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TERMINAL (ENTER 1, 2, 3, OR ?):2

\* \* \* \* \* Welcome to STN International \* \* \* \* \*

NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	MAR 31	IFICDB, IFIPAT, and IFIUDB enhanced with new custom IPC display formats
NEWS	3	MAR 31	CAS REGISTRY enhanced with additional experimental spectra
NEWS	4	MAR 31	CA/CAPplus and CASREACT patent number format for U.S. applications updated
NEWS	5	MAR 31	LPCI now available as a replacement to LDPCI
NEWS	6	MAR 31	EMBASE, EMBAL, and LEMBASE reloaded with enhancements
NEWS	7	APR 04	STN AnaVist, Version 1, to be discontinued
NEWS	8	APR 15	WPIDS, WPINDEX, and WPIX enhanced with new predefined hit display formats
NEWS	9	APR 28	EMBASE Controlled Term thesaurus enhanced
NEWS	10	APR 28	IMSRESEARCH reloaded with enhancements
NEWS	11	MAY 30	INPAFAMDB now available on STN for patent family searching
NEWS	12	MAY 30	DGENE, PCTGEN, and USGENE enhanced with new homology sequence search option
NEWS	13	JUN 06	EPFULL enhanced with 260,000 English abstracts
NEWS	14	JUN 06	KOREAPAT updated with 41,000 documents
NEWS	15	JUN 13	USPATFULL and USPAT2 updated with 11-character patent numbers for U.S. applications
NEWS	16	JUN 19	CAS REGISTRY includes selected substances from web-based collections
NEWS	17	JUN 25	CA/CAPplus and USPAT databases updated with IPC reclassification data
NEWS	18	JUN 30	AEROSPACE enhanced with more than 1 million U.S. patent records
NEWS	19	JUN 30	EMBASE, EMBAL, and LEMBASE updated with additional options to display authors and affiliated organizations
NEWS	20	JUN 30	STN on the Web enhanced with new STN AnaVist Assistant and BLAST plug-in
NEWS	21	JUN 30	STN AnaVist enhanced with database content from EPFULL
NEWS	22	JUL 28	CA/CAPplus patent coverage enhanced
NEWS	23	JUL 28	EPFULL enhanced with additional legal status information from the epoline Register
NEWS	24	JUL 28	IFICDB, IFIPAT, and IFIUDB reloaded with enhancements
NEWS	25	JUL 28	STN Viewer performance improved

NEWS EXPRESS JUNE 27 08 CURRENT WINDOWS VERSION IS V8.3,  
AND CURRENT DISCOVER FILE IS DATED 23 JUNE 2008.

NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS LOGIN	Welcome Banner and News Items
NEWS IPC8	For general information regarding STN implementation of IPC 8

Enter NEWS followed by the item number or name to see news on that specific topic.

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\* \* \* \* \* STN Columbus \* \* \* \* \*

FILE 'HOME' ENTERED AT 07:41:34 ON 29 JUL 2008

=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.21

0.21

FILE 'CAPLUS' ENTERED AT 07:41:46 ON 29 JUL 2008

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FILE COVERS 1907 - 29 Jul 2008 VOL 149 ISS 5

FILE LAST UPDATED: 28 Jul 2008 (20080728/ED)

Caplus now includes complete International Patent Classification (IPC) reclassification data for the second quarter of 2008.

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/legal/infopolicy.html>

=> s 20050080133

L1 0 20050080133

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=> s US 20050080133 A1

126807 US

0 20050080133

69228 A1

L2 0 US 20050080133 A1

(US(W)20050080133(W)A1)

=> s US 20050080133

126807 US

0 20050080133

L3 0 US 20050080133

(US(W)20050080133)

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L5          1 US20050080133/PN
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E1 THROUGH E97 ASSIGNED
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=> file reg
COST IN U.S. DOLLARS                SINCE FILE      TOTAL
                                     ENTRY      SESSION
FULL ESTIMATED COST                30.49        30.70
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FILE 'REGISTRY' ENTERED AT 07:58:33 ON 29 JUL 2008  
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Property values tagged with IC are from the ZIC/VINITI data file  
provided by InfoChem.

STRUCTURE FILE UPDATES: 28 JUL 2008 HIGHEST RN 1036756-19-0  
DICTIONARY FILE UPDATES: 28 JUL 2008 HIGHEST RN 1036756-19-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 9, 2008.

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and  
predicted properties as well as tags indicating availability of  
experimental property data in the original document. For information  
on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

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L6

97 (116532-03-7/BI OR 143193-31-1/BI OR 143218-70-6/BI OR 14470-28-1/BI OR 1639-45-8/BI OR 17305-07-6/BI OR 19971-47-2/BI OR 199999-60-5/BI OR 205944-50-9/BI OR 207621-35-0/BI OR 254887-79-1/BI OR 27570-20-3/BI OR 27686-35-7/BI OR 31702-65-5/BI OR 3245-38-3/BI OR 325124-43-4/BI OR 325124-44-5/BI OR 325124-45-6/BI OR 325124-46-7/BI OR 325124-47-8/BI OR 325124-48-9/BI OR 325124-49-0/BI OR 325124-50-3/BI OR 325124-51-4/BI OR 325124-52-5/BI OR 325124-53-6/BI OR 325124-54-7/BI OR 325124-55-8/BI OR 325124-56-9/BI OR 325124-57-0/BI OR 325124-58-1/BI OR 325124-59-2/BI OR 325124-60-5/BI OR 325124-61-6/BI OR 325124-62-7/BI OR 325124-63-8/BI OR 325124-64-9/BI OR 325124-65-0/BI OR 325124-66-1/BI OR 325124-67-2/BI OR 325124-68-3/BI OR 325124-69-4/BI OR 325124-70-7/BI OR 325124-71-8/BI OR 325124-72-9/BI OR 325124-73-0/BI OR 325124-

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=> file caplus

COST IN U.S. DOLLARS

SINCE FILE

TOTAL

ENTRY

SESSION

FULL ESTIMATED COST

0.46

31.16

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FILE COVERS 1907 - 29 Jul 2008 VOL 149 ISS 5

FILE LAST UPDATED: 28 Jul 2008 (20080728/ED)

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=> s 16

L7 9880 L6

=> s 16 and bone

9880 L6

231445 BONE

L8 2598 L6 AND BONE

=> s 18 and trance/rank

'RANK' IS NOT A VALID FIELD CODE

0 TRANCE/RANK

L9 0 L8 AND TRANCE/RANK

=> s 18 and trance and rank and inhibitor

610 TRANCE

31351 RANK

585573 INHIBITOR

L10 9 L8 AND TRANCE AND RANK AND INHIBITOR

=> dscan 1-10

DSCAN IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.

For a list of commands available to you in the current file, enter "HELP COMMANDS" at an arrow prompt (=>).

=> dscan 1-9

DSCAN IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> dscan

DSCAN IS NOT A RECOGNIZED COMMAND

The previous command name entered was not recognized by the system.  
For a list of commands available to you in the current file, enter  
"HELP COMMANDS" at an arrow prompt (=>).

=> d l10 1-9 hitstr abs ibib

L10 ANSWER 1 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoprotegerin 207621-35-0, TRANCE

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(single-chain multivalent binding proteins with effector function for  
treating various disease including cancer, inflammation, autoimmune  
disease and infection)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 207621-35-0 CAPLUS

CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

AB Multivalent binding peptides, including bi-specific binding peptides,  
having Ig effector function are provided, along with encoding nucleic  
acids, vectors and host cells as well as methods for making such peptides  
and methods for using such peptides to treat or prevent a variety of  
diseases, disorders or conditions, as well as to ameliorate at least one  
symptom associated with such a disease, disorder or condition. The  
bispecific, single chain antibodies comprising a first and second binding  
domains recognizing targets selected from the group consisting of a tumor  
antigen, B cell target, TNF receptor superfamily member, Hedgehog family  
member, receptor tyrosine kinase, proteoglycan-related mol., TGF- $\beta$   
superfamily member, Wnt-related mol., receptor ligand, T cell target,  
dendritic cell target, NK cell target, monocyte/macrophage target and/or  
angiogenesis target.

ACCESSION NUMBER: 2007:1454421 CAPLUS

DOCUMENT NUMBER: 148:99102

TITLE: Single-chain multivalent binding proteins with  
effector function for treating various disease  
including cancer, inflammation, autoimmune disease and  
infection

INVENTOR(S): Thompson, Peter Armstrong; Ledbetter, Jeffrey A.;  
Hayden-Ledbetter, Martha Susan; Grosmaire, Laura Sue;  
Bader, Robert; Brady, William; Tchistiakova,  
Lioudmila; Follettie, Maximillian T.; Calabro,  
Valerie; Schuler, Alwin

PATENT ASSIGNEE(S): Trubion Pharmaceuticals, USA

SOURCE: PCT Int. Appl., 284pp., which  
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2007146968	A2	20071221	WO 2007-US71052	20070612



WO 2007146968 A3 20080619

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.:

US 2006-813261P

P 20060612

US 2006-853287P

P 20061020

L10 ANSWER 2 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

IT 207621-35-0, RANK ligand

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(Id helix-loop-helix proteins neg. regulate TRANCE-mediated osteoclast differentiation)

RN 207621-35-0 CAPLUS

CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

AB Tumor necrosis factor (TNF)-related activation-induced cytokine (TRANCE) induces osteoclast formation from monocyte/macrophage lineage cells via various transcription factors, including the M transcription factor (Mitf). Here, the authors show that inhibitors of differentiation/DNA binding (Ids), helix-loop-helix (HLH) transcription factors, neg. regulate TRANCE-induced osteoclast differentiation. Expression levels of Id1, Id2, and Id3 genes are significantly reduced by TRANCE during osteoclastogenesis. Interestingly, overexpression of the 3 Id genes in bone marrow-derived monocyte/macrophage lineage cells (BMMs) inhibits the formation of tartrate-resistant acid phosphatase (TRAP)-pos. multinuclear osteoclasts, but it does not alter the ability of BMMs to either phagocytose or differentiate into dendritic cells (DCs). Overexpression of Id2 in BMMs attenuates the gene induction of nuclear factor of activated T cells c1 (NFATc1) and osteoclast-associated receptor (OSCAR) during TRANCE-mediated osteoclastogenesis. Furthermore, Id proteins interact with Mitf, a basic HLH (bHLH) transcription factor, and inhibit its transactivation of OSCAR, which is a costimulatory receptor expressed by osteoclast precursors, by attenuating the DNA binding ability of Mitf to the E-box site of the OSCAR promoter. Taken together, the authors' results reveal both a new facet of neg. regulation, mediated by Id proteins, as well as the mechanism whereby TRANCE signaling overcomes it, allowing osteoclastogenesis to proceed.

ACCESSION NUMBER: 2006:336683 CAPLUS

DOCUMENT NUMBER: 144:449213

TITLE: Id helix-loop-helix proteins negatively regulate TRANCE-mediated osteoclast differentiation

AUTHOR(S): Lee, Junwon; Kim, Kabsun; Kim, Jung Ha; Jin, Hye Mi; Choi, Han Kyung; Lee, Seoung-Hoon; Kook, Hyun; Kim, Kyung Keun; Yokota, Yoshifumi; Lee, Soo Young; Choi, Yongwon; Kim, Nacksung

CORPORATE SOURCE: Medical Research Center for Gene Regulation, Chonnam National University Medical School, Gwangju, S. Korea

SOURCE: Blood (2006), 107(7), 2686-2693

CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER: American Society of Hematology

DOCUMENT TYPE: Journal

LANGUAGE: English  
REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 205944-50-9, Osteoprotegerin 207621-35-0, TRANCE  
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(methods for differentiating stem cells using self-replicating  
neocentromeric artificial chromosome with chromatin domains expressing  
transgenes for gene therapy)  
RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
RN 207621-35-0 CAPLUS  
CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
AB The present invention relates to the field of tissue engineering and  
genetic manipulation of cells and to methods for generating tissue  
suitable for use in repair, replacement, rejuvenation or augmentation  
therapy. The present invention contemplates a method for genetically  
manipulating a stem cell by introducing a nucleic acid mol. comprising a  
centromere or neo-centromere into the stem cell, wherein the nucleic acid  
mol. conveys genetic information which is capable of introducing to or  
modifying a trait within the stem cell or progeny of the stem cell such as  
but not limited to modulating the level of stem cell proliferation,  
differentiation and/or self-renewal. The neo-centromere is devoid of  
 $\alpha$ -satellite repeat DNA. One aspect of the present invention  
provides a stem cell comprising a self-replicating artificial chromosome  
with a neo-centromere having centromeric chromatin domains comprising  
expressible genetic material which modifies or introduces at least one  
trait in said stem cell. Microarray gene expression profiles were  
conducted for human 10q25 centromeric region. The engineered stem cells  
may also be re-programmed, for example, to direct the cells down a  
different cell lineage.

ACCESSION NUMBER: 2005:395470 CAPLUS  
DOCUMENT NUMBER: 142:442896  
TITLE: Methods for differentiating stem cells using a  
self-replicating neocentromeric artificial chromosome  
with chromatin domains expressing transgenes for gene  
therapy  
INVENTOR(S): Choo, Kong-Hong Andy; Wong, Lee Hwa; Saffery, Richard  
Eric  
PATENT ASSIGNEE(S): Murdoch Childrens Research Institute, Australia  
SOURCE: PCT Int. Appl., 168 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2005040391	A1	20050506	WO 2004-AU1469	20041025
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LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,				
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,				
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,				

AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,  
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,  
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,  
SN, TD, TG

PRIORITY APPLN. INFO.:

AU 2003-905894

A 20031027

REFERENCE COUNT:

3

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

IT 207621-35-0, RANKL

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(VEGF up-regulation of RANK expression in vascular  
endothelial cells and concomitant increase of angiogenic responses to  
RANKL and mechanisms thereof)

RN 207621-35-0 CAPLUS

CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

AB Vascular endothelial growth factor (VEGF) is known as a key regulator of  
angiogenesis during endochondral bone formation. Recently, the  
authors demonstrated that TNF-related activation-induced cytokine (   
TRANCE or RANKL), which is essential for bone  
remodeling, also had an angiogenic activity. Here the authors report that  
VEGF up-regulates expression of receptor activator of NF- $\kappa$  B (   
RANK) and increases angiogenic responses of endothelial cells to  
TRANCE. Treatment of human umbilical vein endothelial cells  
(HUVECs) with VEGF increased both RANK mRNA and surface protein  
expression. Although placenta growth factor specific to VEGF receptor-1  
had no significant effect on RANK expression, inhibition of  
downstream signaling mol.s. of the VEGF receptor-2 (Flk-1/KDR) such as Src,  
phospholipase C, protein kinase C, and phosphatidylinositol 3'-kinase  
suppressed VEGF-stimulated RANK expression in HUVECs. Moreover,  
the MEK inhibitor PD98059 or expression of dominant neg. MEK1  
inhibited induction of RANK by VEGF but not the Ca<sup>2+</sup> chelator  
BAPTA-acetoxymethyl ester (BAPTA-AM). VEGF potentiated TRANCE  
-induced ERK activation and tube formation via RANK  
up-regulation in HUVECs. Together, these results show that VEGF enhances  
RANK expression in endothelial cells through Flk-1/KDR-protein  
kinase C-ERK signaling pathway, suggesting that VEGF plays an important  
role in modulating the angiogenic action of TRANCE under  
physiol. or pathol. conditions.

ACCESSION NUMBER: 2003:792465 CAPLUS

DOCUMENT NUMBER: 139:302504

TITLE: Vascular endothelial growth factor up-regulates  
expression of receptor activator of NF- $\kappa$ B (   
RANK) in endothelial cells: Concomitant  
increase of angiogenic responses to RANK  
ligand

AUTHOR(S): Min, Jeong-Ki; Kim, Young-Myeong; Kim, Young-Mi; Kim,  
Eok-Cheon; Gho, Yong Song; Kang, Il-Jun; Lee,  
Soo-Young; Kong, Young-Yun; Kwon, Young-Guen

CORPORATE SOURCE: School of Medicine, College of Natural Sciences,  
Department of Biochemistry, Kangwon National  
University, Kangwon-Do, 200-701, S. Korea

SOURCE: Journal of Biological Chemistry (2003), 278(41),  
39548-39557

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular  
Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN  
 IT 207621-35-0, Osteoclast differentiation factor  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (multiple myeloma disruption of TRANCE/osteoprotegerin  
 cytokine axis to trigger bone destruction and promote tumor  
 progression)  
 RN 207621-35-0 CAPLUS  
 CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

AB Bone destruction, caused by aberrant production and activation of osteoclasts, is a prominent feature of multiple myeloma. We demonstrate that myeloma stimulates osteoclastogenesis by triggering a coordinated increase in the tumor necrosis factor-related activation-induced cytokine (TRANCE) and decrease in its decoy receptor, osteoprotegerin (OPG). Immunohistochem. and in situ hybridization studies of bone marrow specimens indicate that in vivo, deregulation of the TRANCE-OPG cytokine axis occurs in myeloma, but not in the limited plasma cell disorder monoclonal gammopathy of unknown significance or in nonmyeloma hematol. malignancies. In coculture, myeloma cell lines stimulate expression of TRANCE and inhibit expression of OPG by stromal cells. Osteoclastogenesis, the functional consequence of increased TRANCE expression, is counteracted by addition of a recombinant TRANCE inhibitor, RANK-Fc, to marrow/myeloma cocultures. Myeloma-stroma interaction also has been postulated to support progression of the malignant clone. In the SCID-hu murine model of human myeloma, administration of RANK-Fc both prevents myeloma-induced bone destruction and interferes with myeloma progression. Our data identify TRANCE and OPG as key cytokines whose deregulation promotes bone destruction and supports myeloma growth.

ACCESSION NUMBER: 2001:729012 CAPLUS  
 DOCUMENT NUMBER: 136:35567  
 TITLE: Multiple myeloma disrupts the TRANCE  
 /osteoprotegerin cytokine axis to trigger bone  
 destruction and promote tumor progression  
 AUTHOR(S): Pearse, Roger N.; Sordillo, Emilia M.; Yaccoby,  
 Shmuel; Wong, Brian R.; Liau, Deng F.; Colman,  
 Neville; Michaeli, Joseph; Epstein, Joshua; Choi,  
 Yongwon  
 CORPORATE SOURCE: Laboratorie of Molecular Genetics, The Rockefeller  
 University, New York, NY, 10021, USA  
 SOURCE: Proceedings of the National Academy of Sciences of the  
 United States of America (2001), 98(20), 11581-11586  
 CODEN: PNASA6; ISSN: 0027-8424  
 PUBLISHER: National Academy of Sciences  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English  
 REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 6 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN  
 IT 205944-50-9, Osteoprotegerin  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (osteoprotegerin and RANKL regulate osteoclast formation by cells in  
 human rheumatoid arthritic joint)  
 RN 205944-50-9 CAPLUS  
 CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

AB This study investigated the involvement of the recently identified regulators of osteoclast formation RANKL [receptor activator of nuclear factor kappa B (RANK) ligand, osteoclast differentiation factor, TRANCE, osteoprotegerin/osteoprotegerin ligand] and its natural inhibitor, osteoprotegerin (OPG), in the bone erosion of rheumatoid arthritis (RA). mRNA was extracted from cells isolated from the pannus and synovial membrane regions of joints of 11 RA patients. Semiquant. reverse transcription-polymerase chain reaction was carried out, and the isolated cells were also cultured to determine their ability to form osteoclasts. MRNAs encoding RANKL, RANK, OPG and macrophage-colony stimulating factor were expressed by cells isolated from RA joints. In addition, mRNA encoding for tumor necrosis factor apoptosis-inducing ligand and the osteoclast markers tartrate-resistant acid phosphatase and calcitonin receptor were also often expressed. Osteoclasts capable of forming resorption lacunae were generated from cells in the RA joints. At 50 ng/mL, recombinant OPG completely inhibited the resorptive activity of these cells. There was a significant correlation between the ratio of RANKL mRNA to OPG mRNA and the number of resorption pits produced. These data suggest that RANKL is an essential factor for osteoclast formation by cells in the rheumatic joint and that OPG may prevent the bone erosion seen in RA joints.

ACCESSION NUMBER: 2001:550193 CAPLUS  
DOCUMENT NUMBER: 136:198708  
TITLE: Osteoprotegerin and receptor activator of nuclear factor kappa B ligand (RANKL) regulate osteoclast formation by cells in the human Rheumatoid arthritic joint  
AUTHOR(S): Haynes, D. R.; Crotti, T. N.; Loric, M.; Bain, G. I.; Atkins, G. J.; Findlay, D. M.  
CORPORATE SOURCE: Department of Pathology, The University of Adelaide and The Royal Adelaide Hospital, Adelaide, 5000, Australia  
SOURCE: Rheumatology (Oxford, United Kingdom) (2001), 40(6), 623-630  
CODEN: RUMAFK; ISSN: 1462-0324  
PUBLISHER: Oxford University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

IT 199999-60-5 207621-35-0, TRANCE

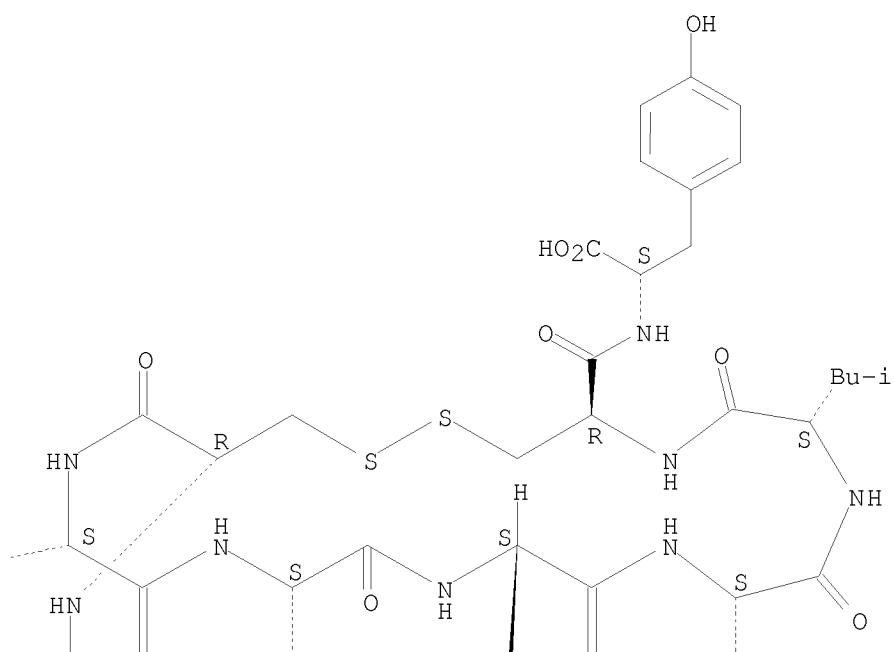
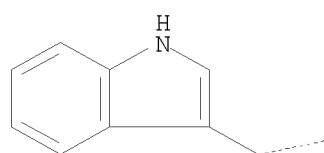
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(inhibition of osteoclastogenesis and activity of osteoclasts with peptide analogs designed from binding loop of TNF receptor superfamily)

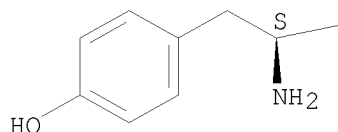
RN 199999-60-5 CAPLUS

CN L-Tyrosine, L-tyrosyl-L-cysteinyl-L-tryptophyl-L-seryl-L-glutaminy-L-tyrosyl-L-leucyl-L-cysteinyl-, cyclic (2→8)-disulfide (9CI) (CA INDEX NAME)

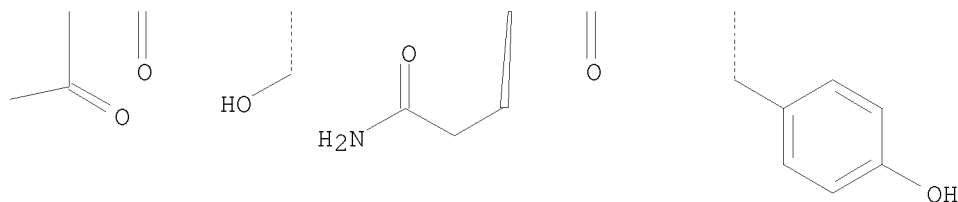
Absolute stereochemistry.



PAGE 2-A



PAGE 2-B



RN 207621-35-0 CAPLUS  
CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

AB Methods of inhibiting osteoclastogenesis and the activity of osteoclasts are disclosed. Methods of treating patients who have diseases characterized bone loss are disclosed. The present invention also provides peptides and peptide analogs designed from a binding loop of a member of the tumor necrosis factor receptor (TNF-R) superfamily. According to the methods, an amount of an inhibitor effective to inhibit osteoclastogenesis is administered to the patient. Methods of modulating dendritic cell maturation, T cell proliferation, and/or CD40 receptor systems in an individual are disclosed. The methods comprise the step of administering to the individual an amount of an inhibitor effective to modulating dendritic cell maturation, T cell proliferation, and/or CD40 receptor systems.

ACCESSION NUMBER: 2001:100993 CAPLUS  
DOCUMENT NUMBER: 134:157588  
TITLE: Methods of inhibiting osteoclastogenesis and the activity of osteoclasts  
INVENTOR(S): Aoki, Kazuhiro; Horne, William Carle; Baron, Roland; Greene, Mark I.; Murali, Ramachandran  
PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA  
SOURCE: PCT Int. Appl., 81 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001008699	A1	20010208	WO 2000-US20510	20000728
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2380009	A1	20010208	CA 2000-2380009	20000728
EP 1221963	A1	20020717	EP 2000-953710	20000728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI, CY  
 JP 2003505514 T 20030212 JP 2001-513429 20000728  
 US 6682739 B1 20040127 US 2000-627775 20000728  
 AU 777634 B2 20041028 AU 2000-66111 20000728  
 PRIORITY APPLN. INFO.: US 1999-146090P P 19990728  
 WO 2000-US20510 W 20000728  
 OTHER SOURCE(S): MARPAT 134:157588  
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN

IT 60-38-8 434-13-9 468-20-2 508-64-5  
 514-39-6 516-55-2 641-83-8 808-19-5  
 963-74-6 971-93-7 1639-45-8 3245-38-3  
 4481-62-3 5218-29-1 6242-26-8  
 7050-16-0 14470-28-1 17305-07-6  
 19971-47-2 27570-20-3 27686-35-7  
 31702-65-5 38775-99-4 39006-74-1  
 40615-36-9 49757-42-8 52552-28-0  
 55706-84-8 56786-63-1 58212-53-6  
 58212-85-4 58952-66-2 58952-69-5  
 72093-15-3 79076-86-1 81913-28-2  
 86610-66-4 89622-53-7 116532-03-7  
 143193-31-1 143218-70-6 199999-60-5  
 205944-50-9, Osteoprotegerin 254887-79-1  
 325124-43-4 325124-44-5 325124-45-6  
 325124-46-7 325124-47-8 325124-48-9  
 325124-49-0 325124-50-3 325124-51-4  
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 325124-55-8 325124-56-9 325124-57-0  
 325124-58-1 325124-59-2 325124-60-5  
 325124-61-6 325124-62-7 325124-63-8  
 325124-64-9 325124-65-0 325124-66-1  
 325124-67-2 325124-68-3 325124-69-4  
 325124-70-7 325124-71-8 325124-72-9  
 325124-73-0 325124-74-1 325124-75-2  
 325124-76-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

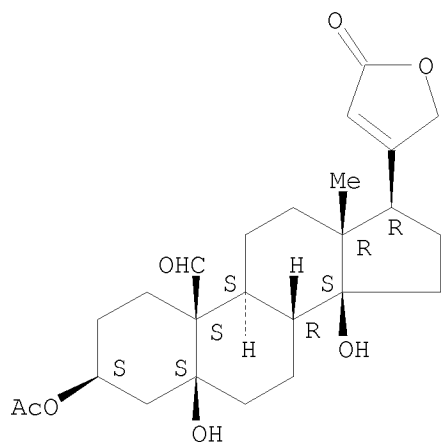
(methods of inhibiting osteoclast activity using TRANCE/  
 RANK inhibitors and application to prevention of bone  
 loss and treatment of osteoporosis)

RN 60-38-8 CAPLUS

CN Card-20(22)-enolide, 3-(acetyloxy)-5,14-dihydroxy-19-oxo-,  
 (3 $\beta$ ,5 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

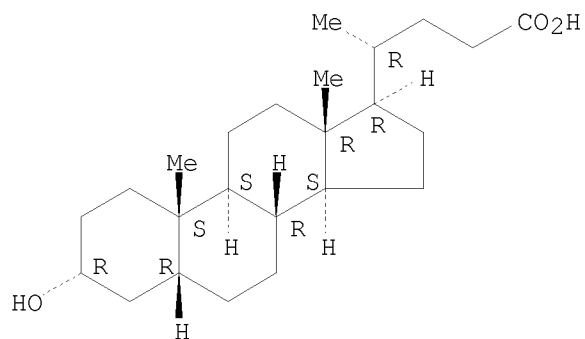




RN 434-13-9 CAPLUS

CN Cholan-24-oic acid, 3-hydroxy-, (3 $\alpha$ ,5 $\beta$ )- (CA INDEX NAME)

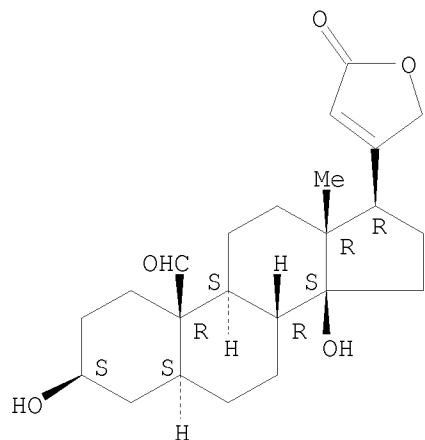
Absolute stereochemistry.



RN 468-20-2 CAPLUS

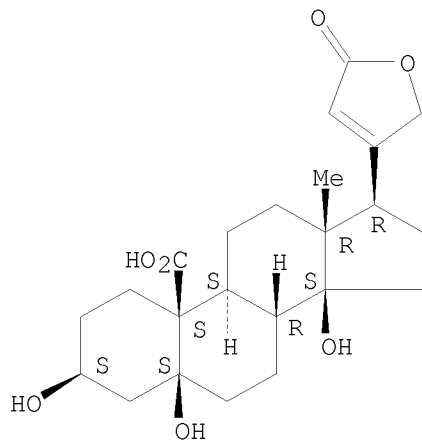
CN Card-20(22)-enolide, 3,14-dihydroxy-19-oxo-, (3 $\beta$ ,5 $\alpha$ )- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



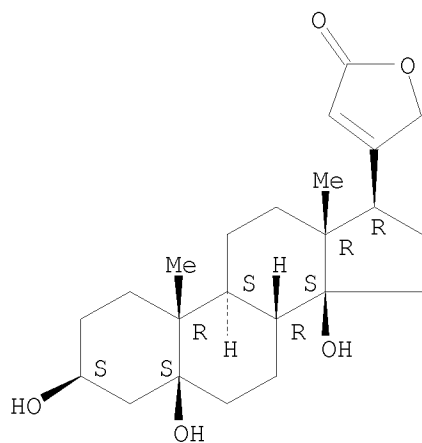
RN 508-64-5 CAPLUS  
 CN 24-Norchol-20(22)-ene-19,23-dioic acid, 3,5,14,21-tetrahydroxy-,  
 $\gamma$ -lactone, (3 $\beta$ ,5 $\beta$ ,14 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.



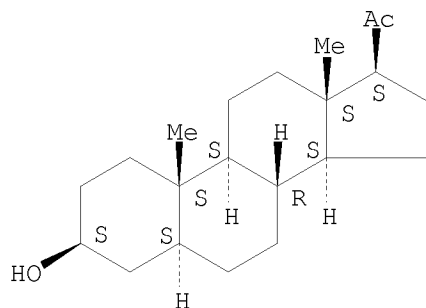
RN 514-39-6 CAPLUS  
 CN Card-20(22)-enolide, 3,5,14-trihydroxy-, (3 $\beta$ ,5 $\beta$ )- (CA INDEX  
 NAME)

Absolute stereochemistry.



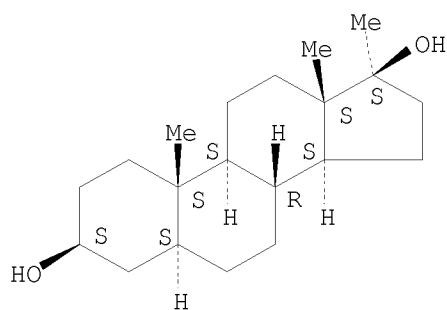
RN 516-55-2 CAPLUS  
 CN Pregnan-20-one, 3-hydroxy-, (3 $\beta$ ,5 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



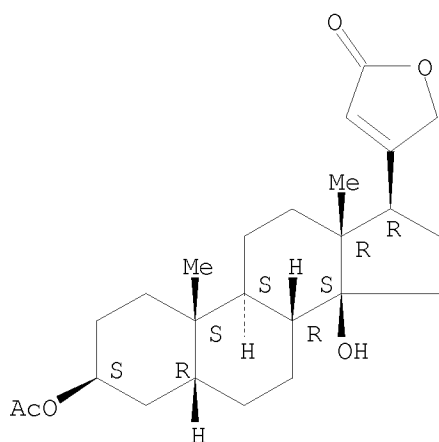
RN 641-83-8 CAPLUS  
 CN Androstane-3,17-diol, 17-methyl-, (3 $\beta$ ,5 $\alpha$ ,17 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.



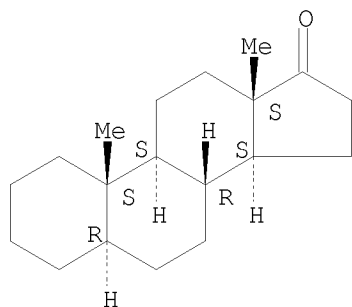
RN 808-19-5 CAPLUS  
 CN Card-20(22)-enolide, 3-(acetyloxy)-14-hydroxy-, (3 $\beta$ ,5 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.

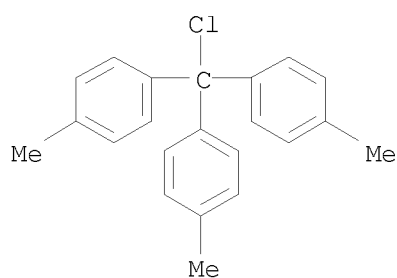


RN 963-74-6 CAPLUS  
 CN Androstan-17-one, (5 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

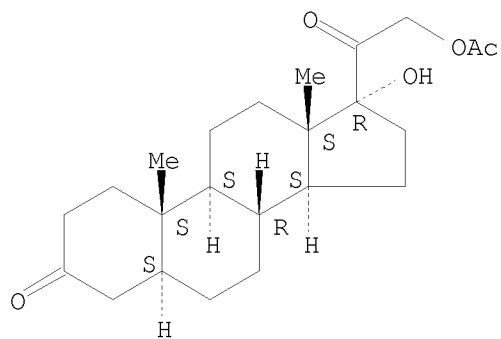


RN 971-93-7 CAPLUS  
 CN Benzene, 1,1',1''-(chloromethylidene)tris[4-methyl- (CA INDEX NAME)



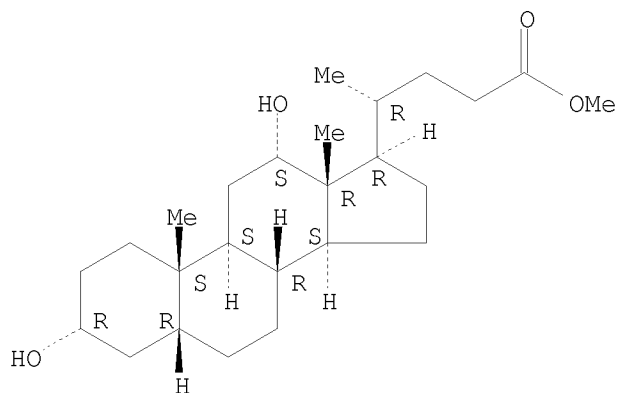
RN 1639-45-8 CAPLUS  
 CN Pregnane-3,20-dione, 21-(acetyloxy)-17-hydroxy-, (5 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



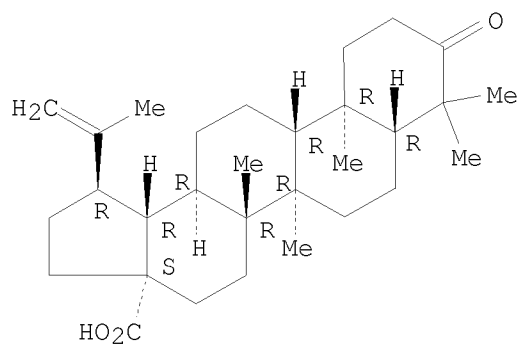
RN 3245-38-3 CAPLUS  
 CN Cholan-24-oic acid, 3,12-dihydroxy-, methyl ester, (3 $\alpha$ ,5 $\beta$ ,12 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



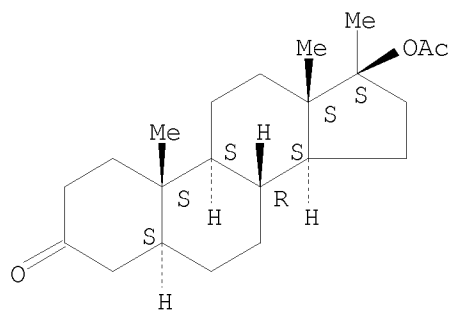
RN 4481-62-3 CAPLUS  
 CN Lup-20(29)-en-28-oic acid, 3-oxo- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



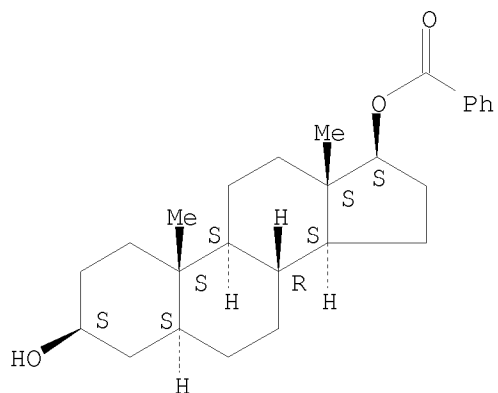
RN 5218-29-1 CAPLUS  
 CN Androstan-3-one, 17-(acetyloxy)-17-methyl-, (5 $\alpha$ ,17 $\beta$ )- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.

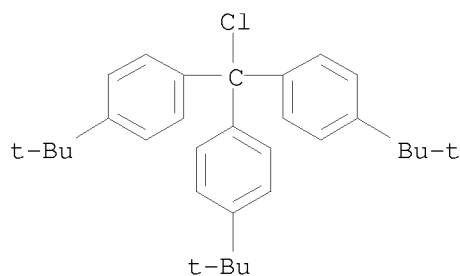


RN 6242-26-8 CAPLUS  
 CN Androstane-3,17-diol, 17-benzoate, (3 $\beta$ ,5 $\alpha$ ,17 $\beta$ )- (9CI) (CA  
 INDEX NAME)

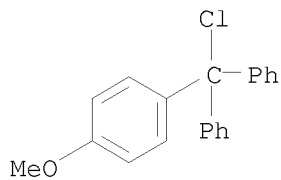
Absolute stereochemistry.



RN 7050-16-0 CAPLUS  
 CN Benzene, 1,1',1''-(chloromethylidene)tris[4-(1,1-dimethylethyl)- (CA INDEX NAME)

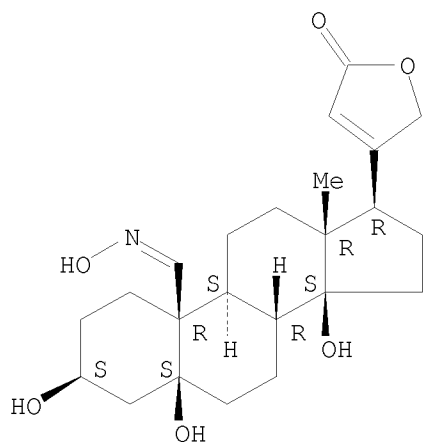


RN 14470-28-1 CAPLUS  
 CN Benzene, 1-(chlorodiphenylmethyl)-4-methoxy- (CA INDEX NAME)



RN 17305-07-6 CAPLUS  
 CN Card-20(22)-enolide, 3,5,14-trihydroxy-19-(hydroxyimino)-, (3 $\beta$ ,5 $\beta$ )- (9CI) (CA INDEX NAME)

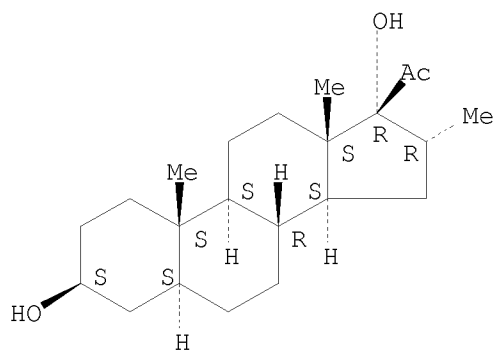
Absolute stereochemistry.  
 Double bond geometry unknown.



RN 19971-47-2 CAPLUS

CN Pregnan-20-one, 3,17-dihydroxy-16-methyl-, (3 $\beta$ ,5 $\alpha$ ,16 $\alpha$ )-  
(9CI) (CA INDEX NAME)

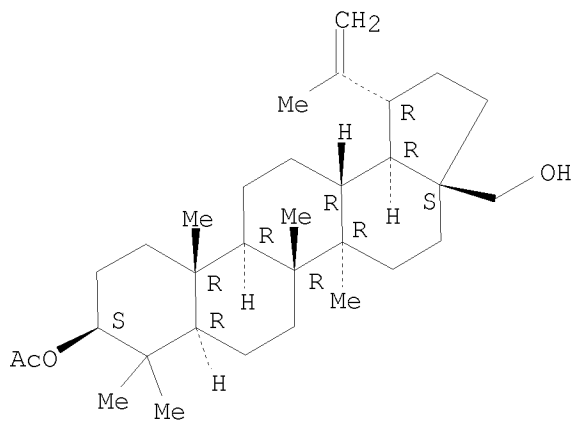
Absolute stereochemistry. Rotation (+).



RN 27570-20-3 CAPLUS

CN Lup-20(29)-ene-3,28-diol, 3-acetate, (3 $\beta$ )- (CA INDEX NAME)

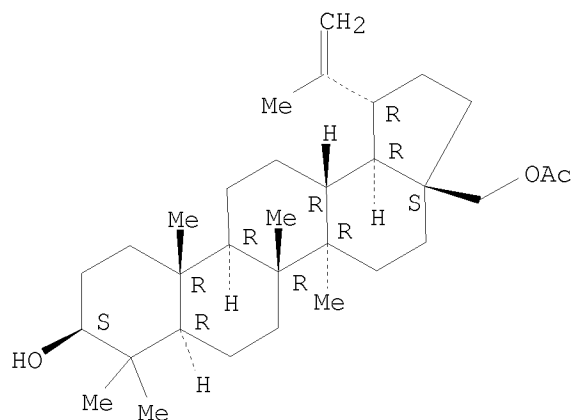
Absolute stereochemistry.



RN 27686-35-7 CAPLUS

CN Lup-20(29)-ene-3,28-diol, 28-acetate, (3 $\beta$ )- (CA INDEX NAME)

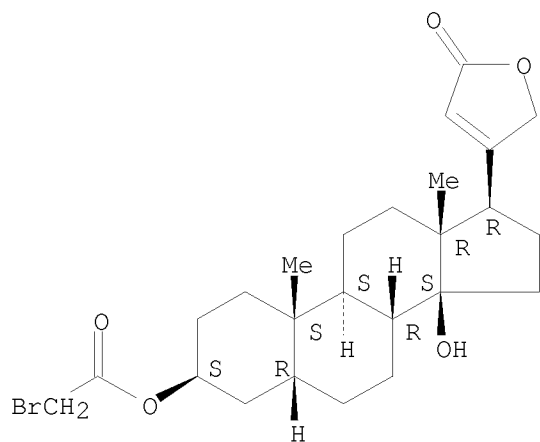
Absolute stereochemistry.



RN 31702-65-5 CAPLUS

CN Card-20(22)-enolide, 3-[(bromoacetyl)oxy]-14-hydroxy-, (3 $\beta$ , 5 $\beta$ )-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.

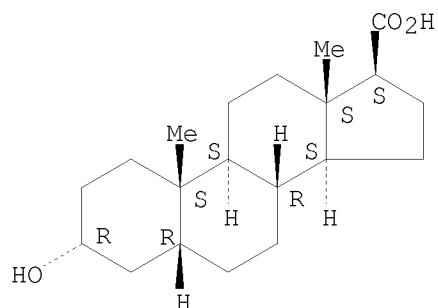


RN 38775-99-4 CAPLUS

CN Androstane-17-carboxylic acid, 3-hydroxy-, (3 $\alpha$ , 5 $\beta$ , 17 $\beta$ )-  
(9CI) (CA INDEX NAME)

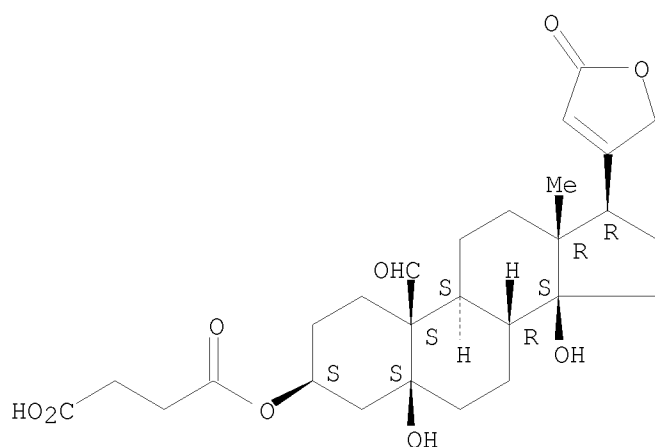
Absolute stereochemistry.



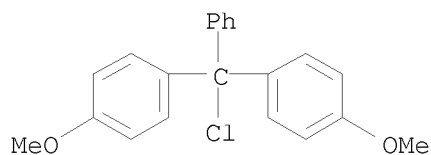


RN 39006-74-1 CAPLUS  
 CN Card-20(22)-enolide, 3-(3-carboxy-1-oxopropoxy)-5,14-dihydroxy-19-oxo-,  
 (3 $\beta$ , 5 $\beta$ )- (9CI) (CA INDEX NAME)

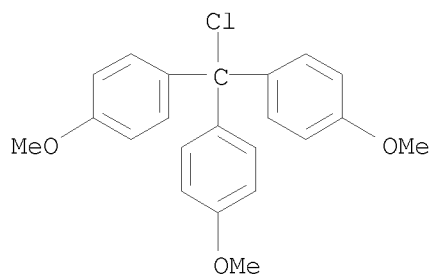
Absolute stereochemistry.



RN 40615-36-9 CAPLUS  
 CN Benzene, 1,1'-(chlorophenylmethylene)bis[4-methoxy- (CA INDEX NAME)

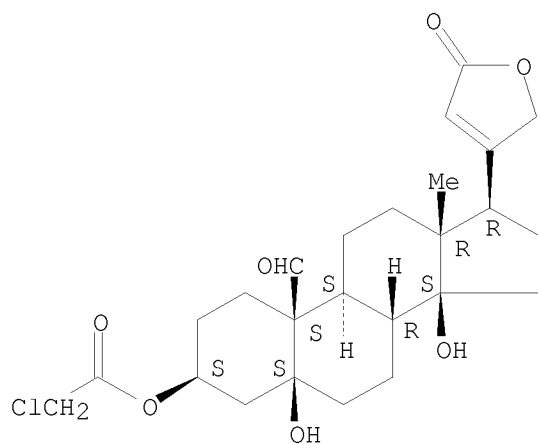


RN 49757-42-8 CAPLUS  
 CN Benzene, 1,1',1''-(chloromethylidyne)tris[4-methoxy- (CA INDEX NAME)



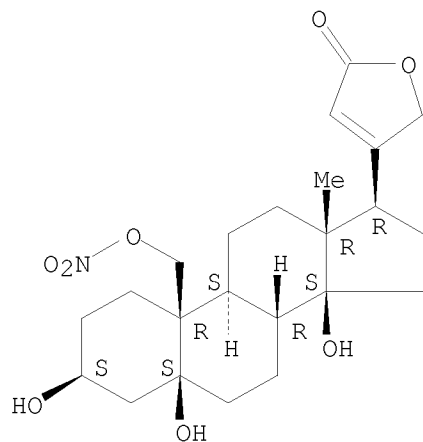
RN 52552-28-0 CAPLUS  
 CN Card-20(22)-enolide, 3-[(chloroacetyl)oxy]-5,14-dihydroxy-19-oxo-,  
 (3 $\beta$ ,5 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 55706-84-8 CAPLUS  
 CN Card-20(22)-enolide, 3,5,14-trihydroxy-19-(nitrooxy)-, (3 $\beta$ ,5 $\beta$ )-  
 (9CI) (CA INDEX NAME)

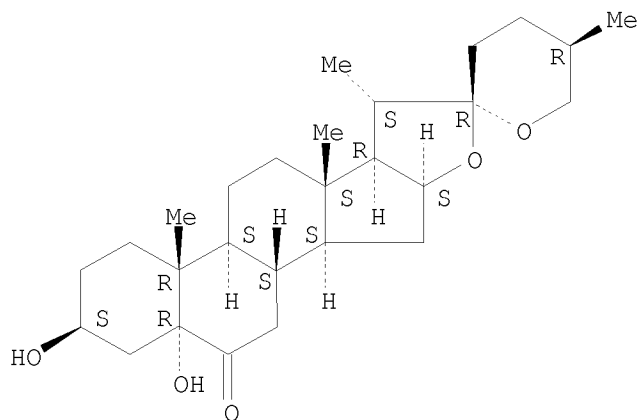
Absolute stereochemistry.



RN 56786-63-1 CAPLUS

CN Spirostan-6-one, 3,5-dihydroxy-, (3 $\beta$ ,5 $\alpha$ ,25R)- (9CI) (CA INDEX NAME)

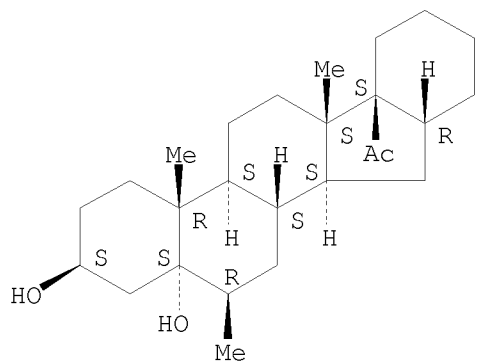
Absolute stereochemistry.



RN 58212-53-6 CAPLUS

CN Ethanone, 1-[(3 $\beta$ ,5 $\alpha$ ,6 $\beta$ ,16 $\beta$ ,17 $\beta$ )-3,5-dihydroxy-6-methyl-16,24-cyclo-21-norcholan-17-yl]- (9CI) (CA INDEX NAME)

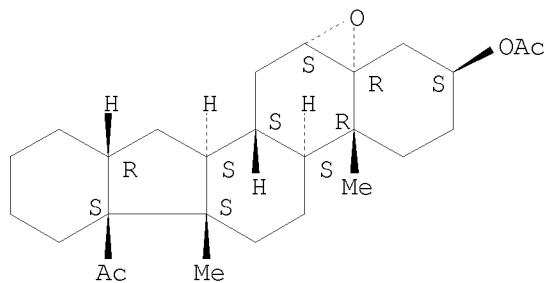
Absolute stereochemistry.



RN 58212-85-4 CAPLUS

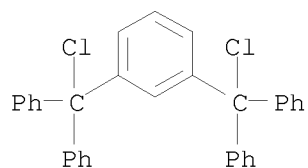
CN Ethanone, 1-[(3 $\beta$ ,5 $\alpha$ ,6 $\alpha$ ,16 $\beta$ ,17 $\beta$ )-3-(acetyloxy)-5,6-epoxy-16,24-cyclo-21-norcholan-17-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



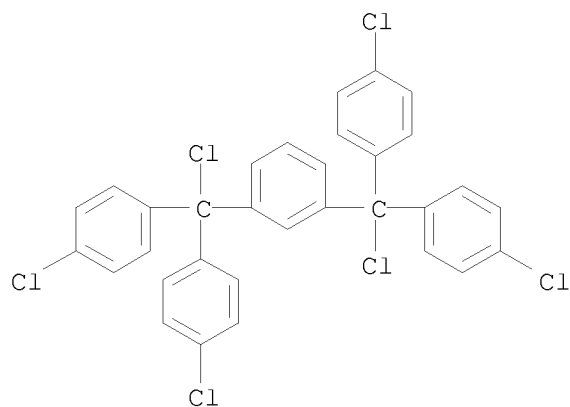
RN 58952-66-2 CAPLUS

CN Benzene, 1,3-bis(chlorodiphenylmethyl)- (CA INDEX NAME)



RN 58952-69-5 CAPLUS

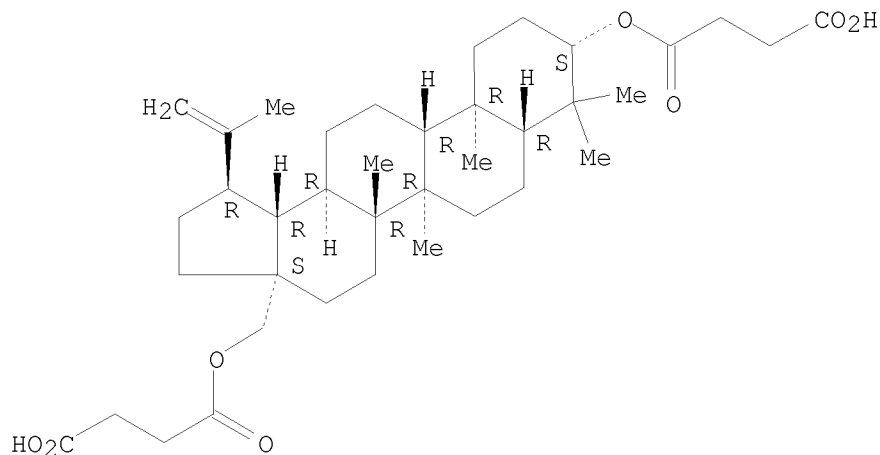
CN Benzene, 1,3-bis[chlorobis(4-chlorophenyl)methyl]- (CA INDEX NAME)



RN 72093-15-3 CAPLUS

CN Lup-20(29)-ene-3,28-diol, 3,28-bis(hydrogen butanedioate), (3 $\beta$ )- (CA INDEX NAME)

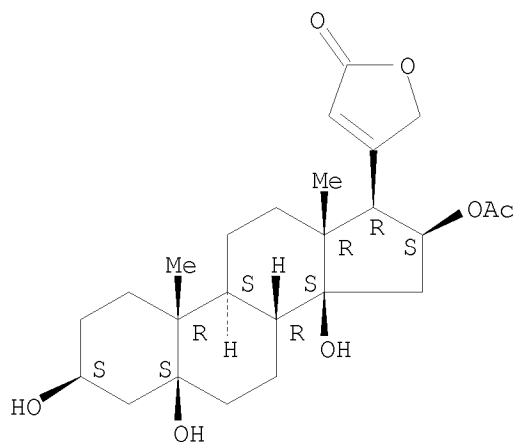
Absolute stereochemistry. Rotation (+).



RN 79076-86-1 CAPLUS

CN Card-20(22)-enolide, 16-(acetyloxy)-3,5,14-trihydroxy-, (3 $\beta$ ,5 $\beta$ ,16 $\beta$ )- (CA INDEX NAME)

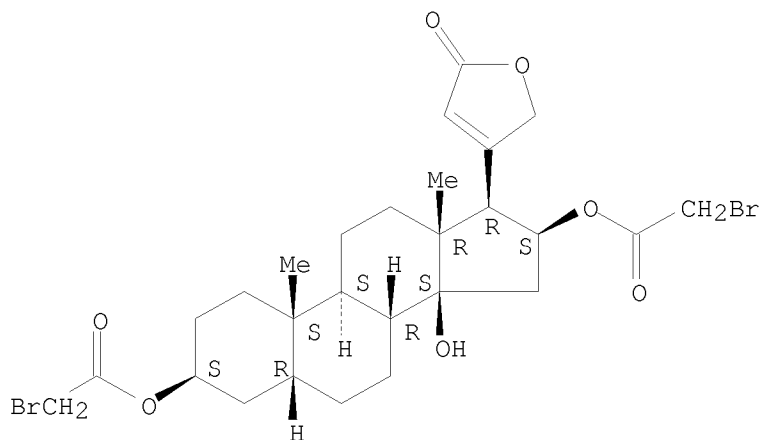
Absolute stereochemistry.



RN 81913-28-2 CAPLUS

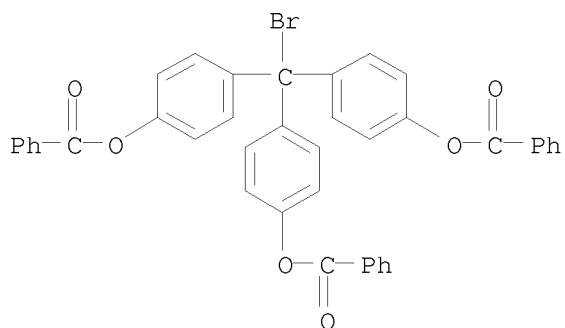
CN Card-20(22)-enolide, 3,16-bis[(bromoacetyl)oxy]-14-hydroxy-,  
(3 $\beta$ , 5 $\beta$ , 16 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 86610-66-4 CAPLUS

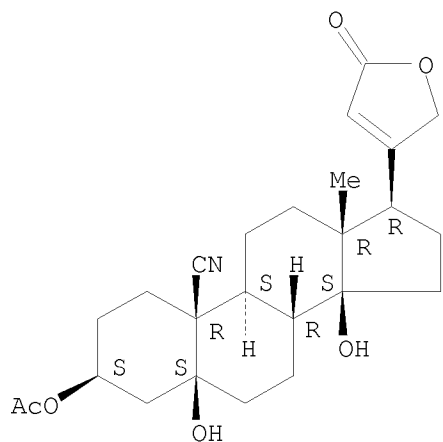
CN Phenol, 4,4',4''-(bromomethylidyne)tris-, tribenzoate (9CI) (CA INDEX  
NAME)



RN 89622-53-7 CAPLUS

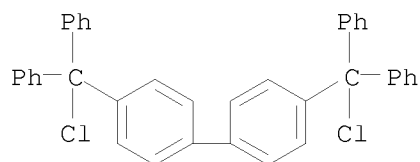
CN 19-Norcard-20(22)-enolide, 3-(acetyloxy)-10-cyano-5,14-dihydroxy-,  
(3 $\beta$ ,5 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



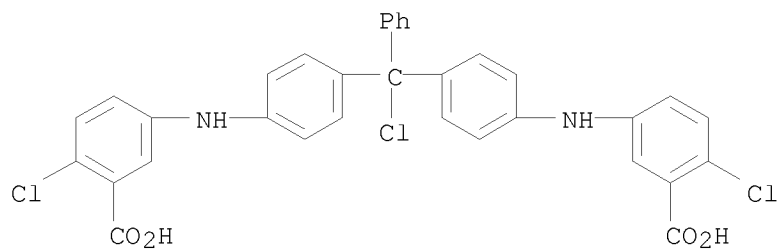
RN 116532-03-7 CAPLUS

CN 1,1'-Biphenyl, 4,4'-bis(chlorodiphenylmethyl)- (CA INDEX NAME)



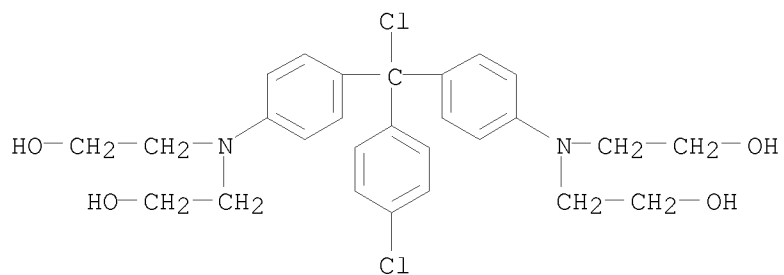
RN 143193-31-1 CAPLUS

CN Benzoic acid, 3,3'-[(chlorophenylmethylene)bis(4,1-phenyleneimino)]bis[6-chloro- (9CI) (CA INDEX NAME)



RN 143218-70-6 CAPLUS

CN Ethanol, 2,2',2'',2'''-[[chloro(4-chlorophenyl)methylene]bis(4,1-phenylenenitrilo)]tetrakis- (9CI) (CA INDEX NAME)

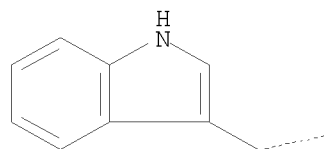


RN 199999-60-5 CAPLUS

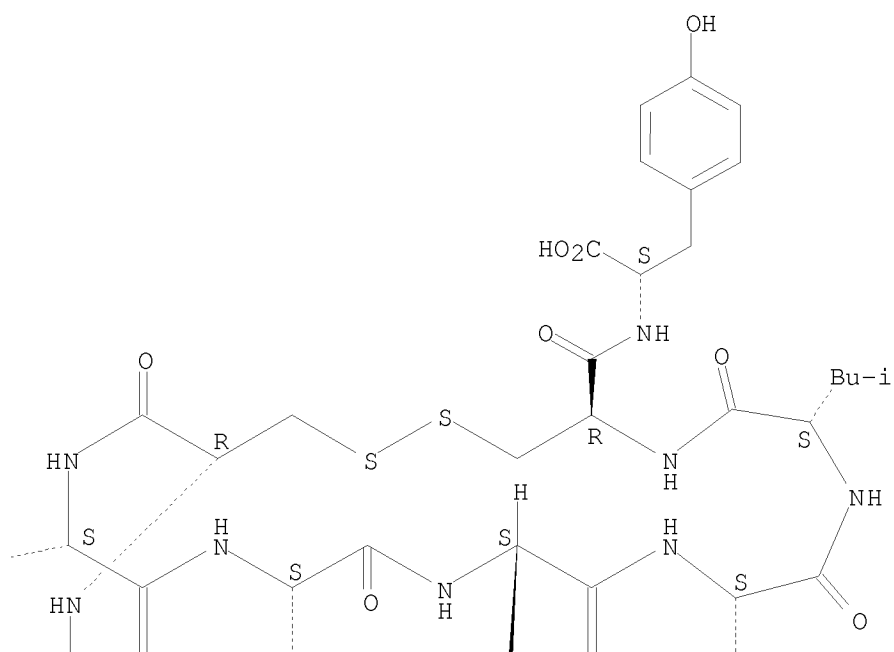
CN L-Tyrosine, L-tyrosyl-L-cysteinyl-L-tryptophyl-L-seryl-L-glutaminyl-L-tyrosyl-L-leucyl-L-cysteinyl-, cyclic (2→8)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

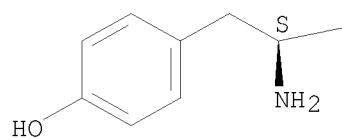
PAGE 1-A



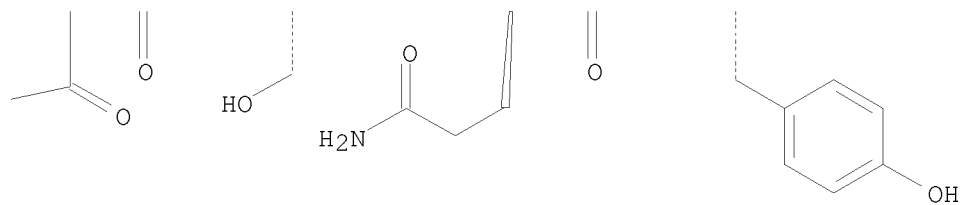
PAGE 1-B



PAGE 2-A



PAGE 2-B

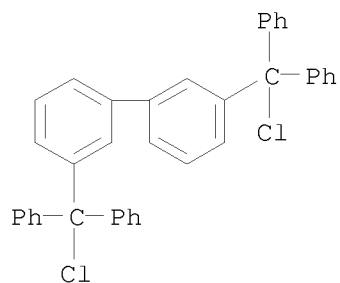


RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

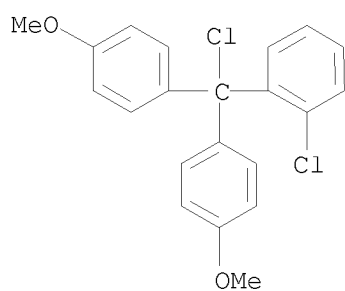
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 254887-79-1 CAPLUS  
CN 1,1'-Biphenyl, 3,3'-bis(chlorodiphenylmethyl)- (CA INDEX NAME)



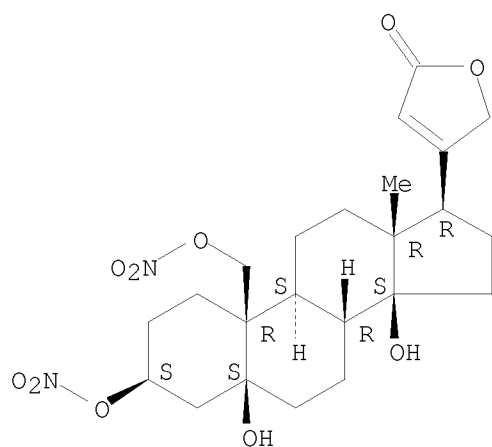


RN 325124-43-4 CAPLUS  
 CN Benzene, 1-chloro-2-[chlorobis(4-methoxyphenyl)methyl]- (CA INDEX NAME)



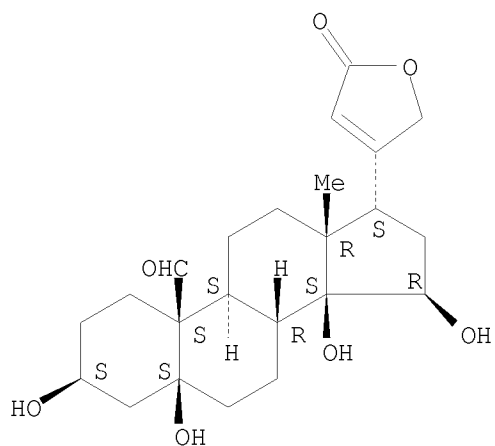
RN 325124-44-5 CAPLUS  
 CN Card-20(22)-enolide, 5,14-dihydroxy-3,19-bis(nitrooxy)-, (3 $\beta$ , 5 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 325124-45-6 CAPLUS  
 CN Card-20(22)-enolide, 3,5,14,15-tetrahydroxy-19-oxo-, (3 $\beta$ , 5 $\beta$ , 15 $\beta$ , 17 $\alpha$ )- (9CI) (CA INDEX NAME)

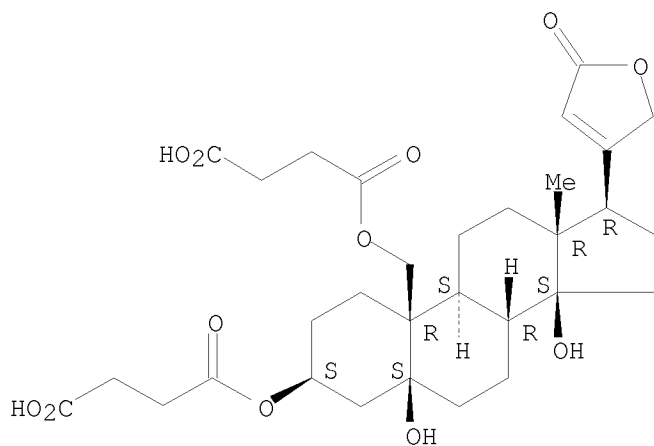
Absolute stereochemistry.



RN 325124-46-7 CAPLUS

CN Card-20(22)-enolide, 3,19-bis(3-carboxy-1-oxopropoxy)-5,14-dihydroxy-,  
(3 $\beta$ , 5 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

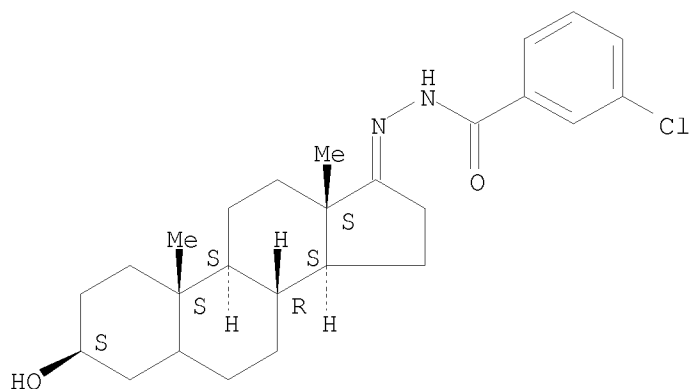


RN 325124-47-8 CAPLUS

CN Benzoic acid, 3-chloro-, [(3 $\beta$ )-3-hydroxyandrost-17-ylidene]hydrazide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

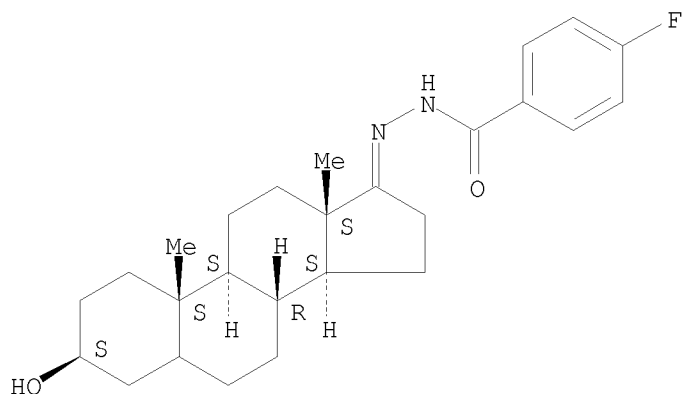
Double bond geometry unknown.



RN 325124-48-9 CAPLUS

CN Benzoic acid, 4-fluoro-, [(3β)-3-hydroxyandrost-17-ylidene]hydrazide (9CI) (CA INDEX NAME)

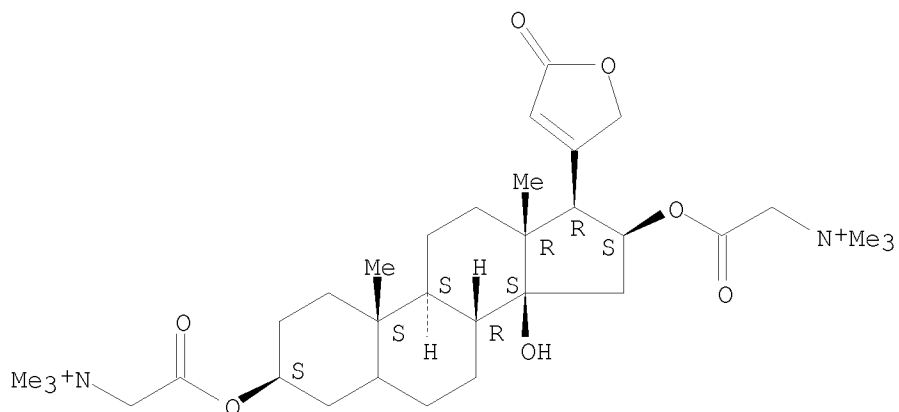
Absolute stereochemistry.  
Double bond geometry unknown.



RN 325124-49-0 CAPLUS

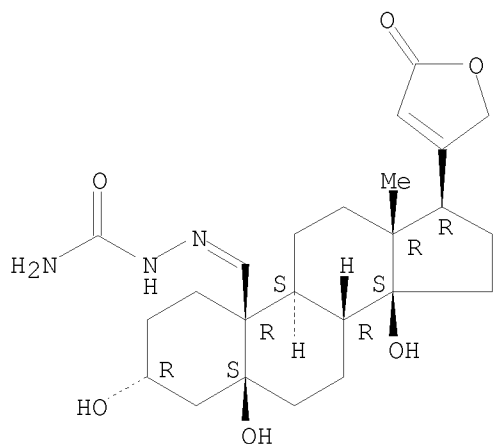
CN Card-20(22)-enolide, 14-hydroxy-3,16-bis[[ (trimethylammonio)acetyl]oxy]-, (3β,16β)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



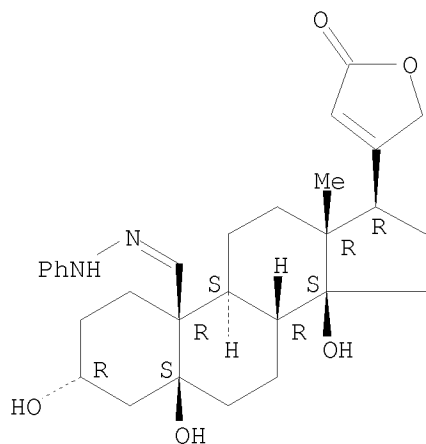
RN 325124-50-3 CAPLUS  
 CN Card-20(22)-enolide, 19-[(aminocarbonyl)hydrazono]-3,5,14-trihydroxy-,  
 (3 $\alpha$ ,5 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



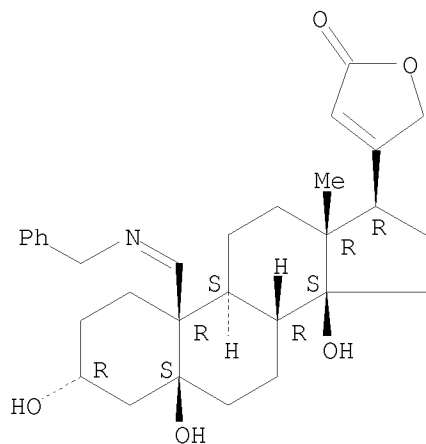
RN 325124-51-4 CAPLUS  
 CN Card-20(22)-enolide, 3,5,14-trihydroxy-19-(phenylhydrazono)-,  
 (3 $\alpha$ ,5 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.  
 Double bond geometry unknown.



RN 325124-52-5 CAPLUS  
 CN Card-20(22)-enolide, 3,5,14-trihydroxy-19-[(phenylmethyl)imino]-,  
 (3 $\alpha$ ,5 $\beta$ )- (9CI) (CA INDEX NAME)

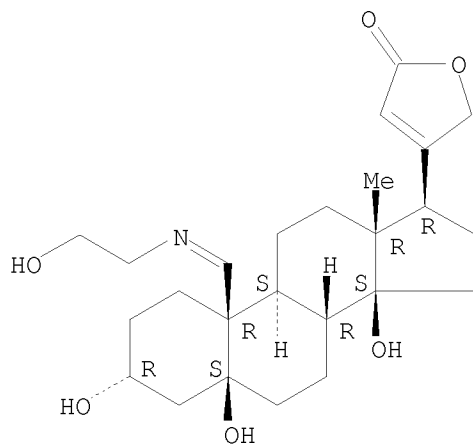
Absolute stereochemistry.  
 Double bond geometry unknown.



RN 325124-53-6 CAPLUS

CN Card-20(22)-enolide, 3,5,14-trihydroxy-19-[(2-hydroxyethyl)imino]-,  
(3 $\alpha$ ,5 $\beta$ )- (9CI) (CA INDEX NAME)

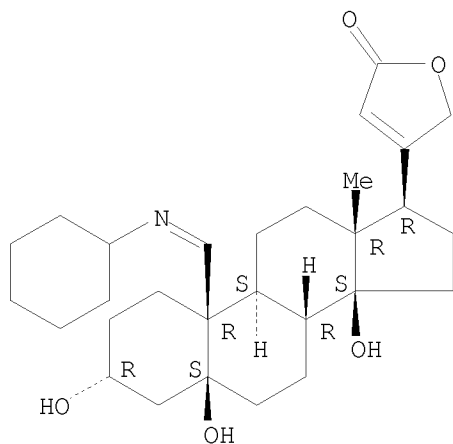
Absolute stereochemistry.  
Double bond geometry unknown.



RN 325124-54-7 CAPLUS

CN Card-20(22)-enolide, 19-(cyclohexylimino)-3,5,14-trihydroxy-,  
(3 $\alpha$ ,5 $\beta$ )- (9CI) (CA INDEX NAME)

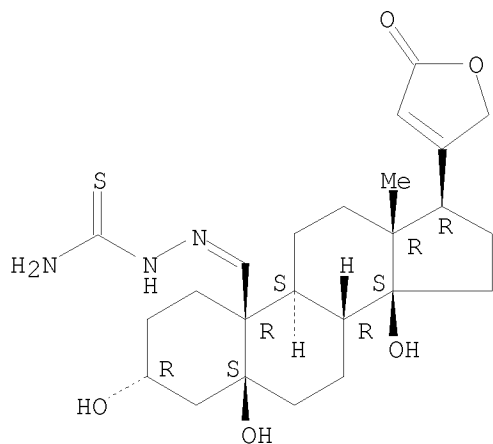
Absolute stereochemistry.  
Double bond geometry unknown.



RN 325124-55-8 CAPLUS

CN Card-20(22)-enolide, 19-[(aminothioxomethyl)hydrazono]-3,5,14-trihydroxy-, (3 $\alpha$ , 5 $\beta$ )- (9CI) (CA INDEX NAME)

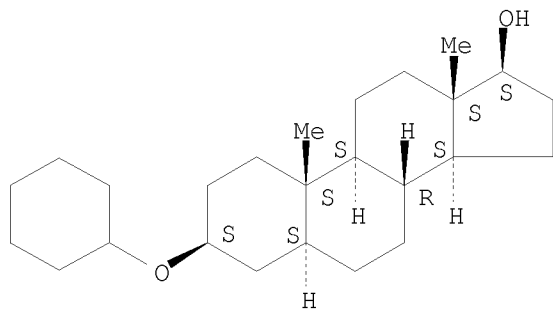
Absolute stereochemistry.  
Double bond geometry unknown.



RN 325124-56-9 CAPLUS

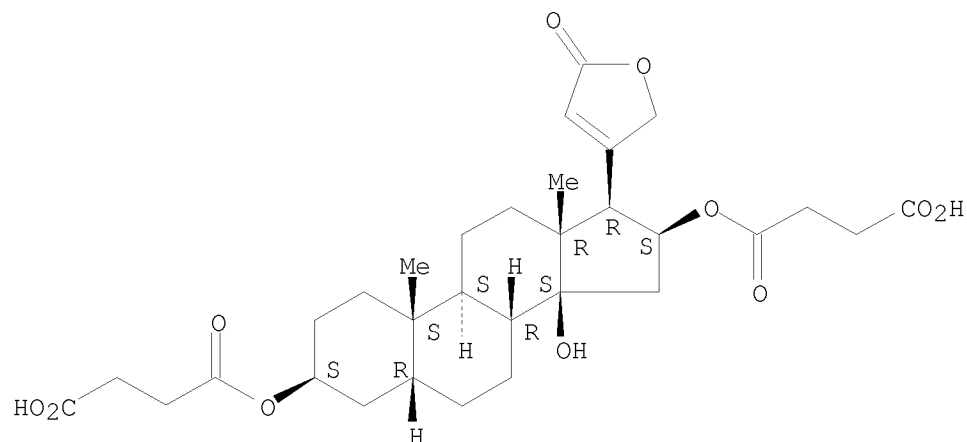
CN Androstan-17-ol, 3-(cyclohexyloxy)-, (3 $\beta$ , 5 $\alpha$ , 17 $\beta$ )- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



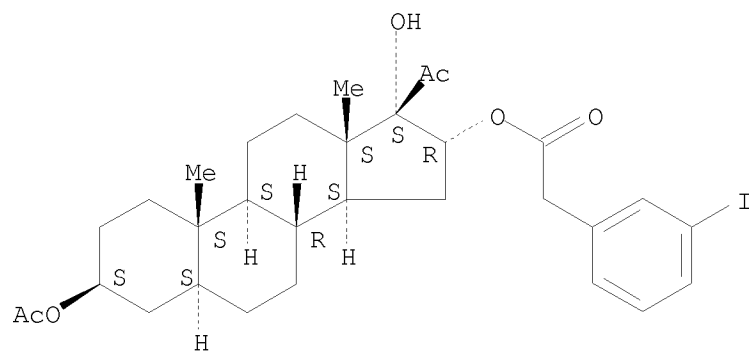
RN 325124-57-0 CAPLUS  
 CN Card-20(22)-enolide, 3,16-bis(3-carboxy-1-oxopropoxy)-14-hydroxy-,  
 (3 $\beta$ ,5 $\beta$ ,16 $\beta$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



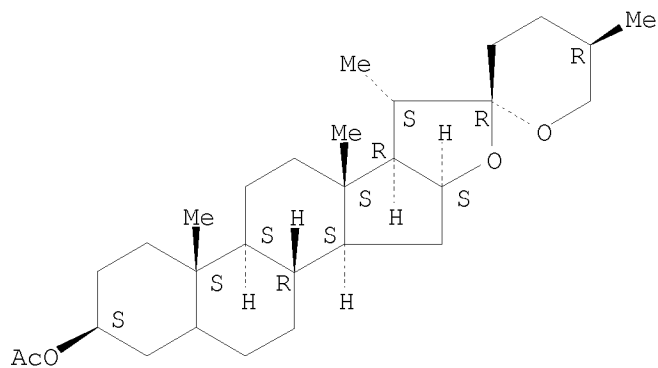
RN 325124-58-1 CAPLUS  
 CN Pregnan-20-one, 3-(acetyloxy)-17-hydroxy-16-[[ (3-iodophenyl)acetyl]oxy]-,  
 (3 $\beta$ ,5 $\alpha$ ,16 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 325124-59-2 CAPLUS  
 CN Spirostan-3-ol, acetate, (3 $\beta$ ,25R)- (9CI) (CA INDEX NAME)

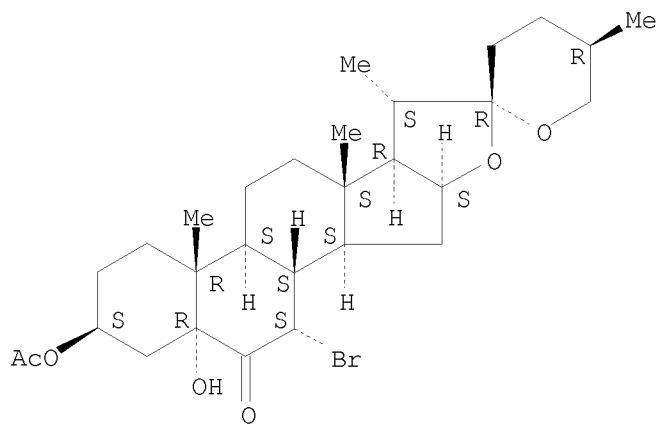
Absolute stereochemistry.



RN 325124-60-5 CAPLUS

CN Spirostan-6-one, 3-(acetyloxy)-7-bromo-5-hydroxy-,  
(3 $\beta$ , 5 $\alpha$ , 7 $\alpha$ , 25R)- (9CI) (CA INDEX NAME)

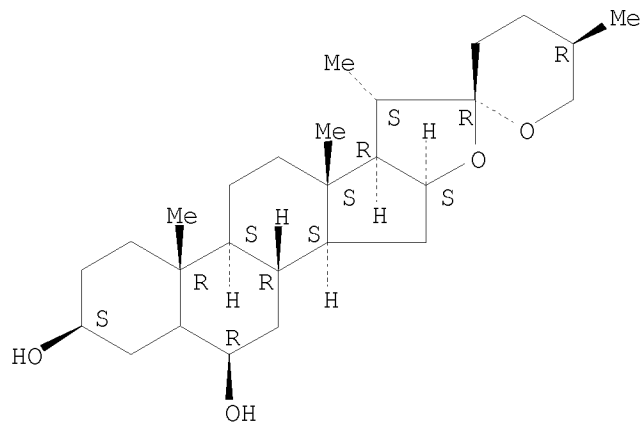
Absolute stereochemistry.



RN 325124-61-6 CAPLUS

CN Spirostan-3,6-diol, (3 $\beta$ , 6 $\beta$ , 25R)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



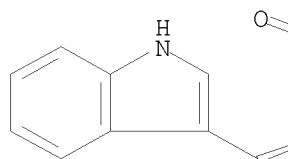
RN 325124-62-7 CAPLUS



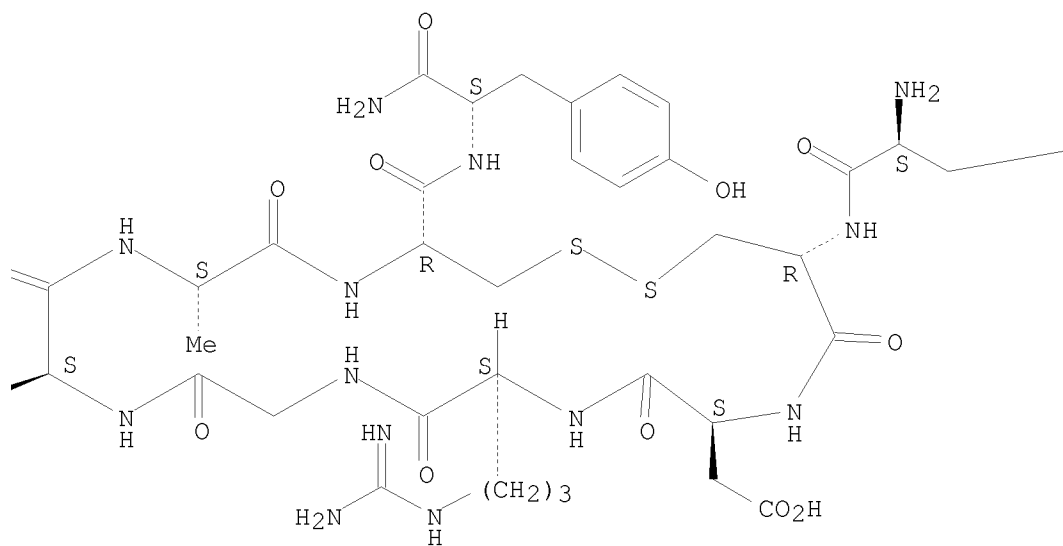
CN L-Tyrosinamide, L-tyrosyl-L-cysteinyl-L- $\alpha$ -aspartyl-L-arginylglycyl-L-tryptophyl-L-alanyl-L-cysteinyl-, cyclic (2 $\rightarrow$ 8)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

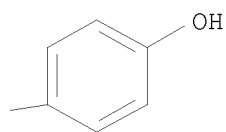
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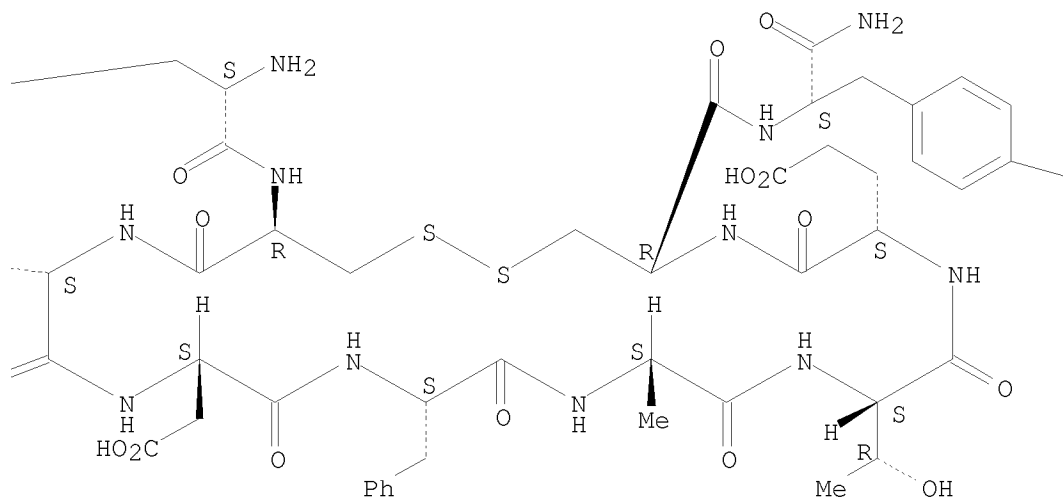
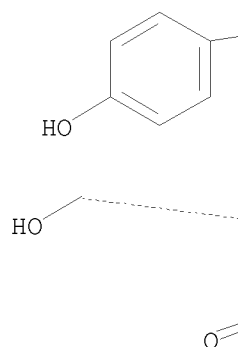
RN 325124-63-8 CAPLUS

Absolute stereochemistry.



RN 325124-64-9 CAPLUS  
 CN L-Tyrosinamide, L-tyrosyl-L-cysteinyl-L-seryl-L- $\alpha$ -aspartyl-L-phenylalanyl-L-alanyl-L-threonyl-L- $\alpha$ -glutamyl-L-cysteinyl-, cyclic (2 $\rightarrow$ 9)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

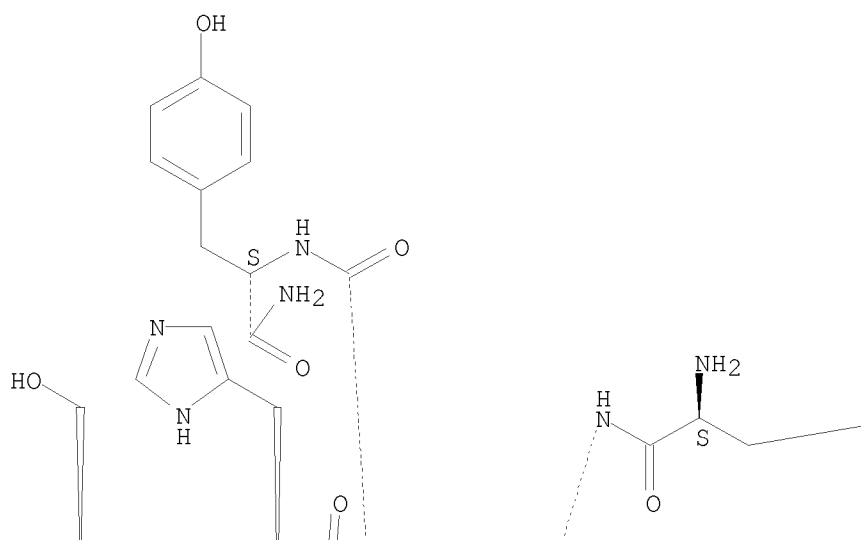


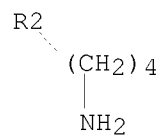
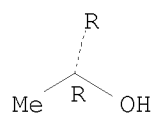
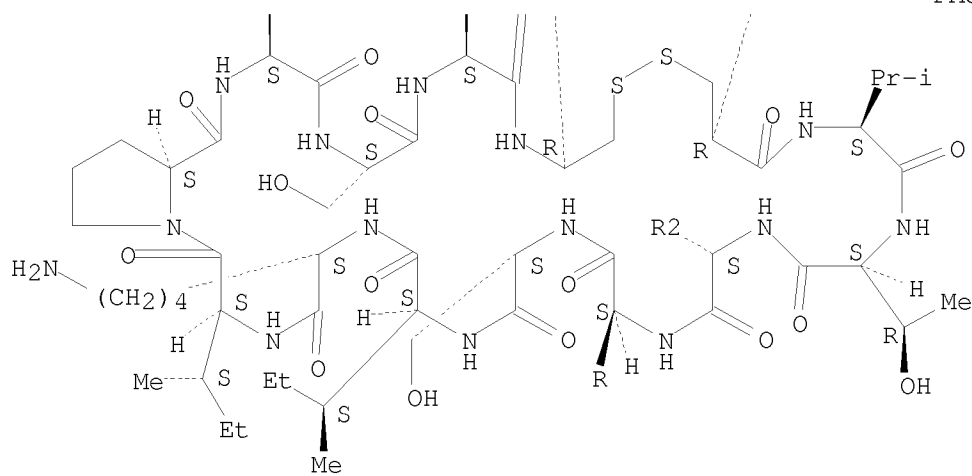
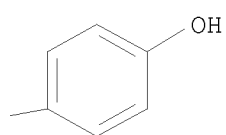
—OH

RN 325124-65-0 CAPLUS

CN L-Tyrosinamide, L-tyrosyl-L-cysteinyl-L-valyl-L-threonyl-L-lysyl-L-threonyl-L-seryl-L-isoleucyl-L-lysyl-L-isoleucyl-L-prolyl-L-seryl-L-seryl-L-histidyl-L-cysteinyl-, cyclic (2→15)-disulfide (9CI) (CA INDEX NAME)

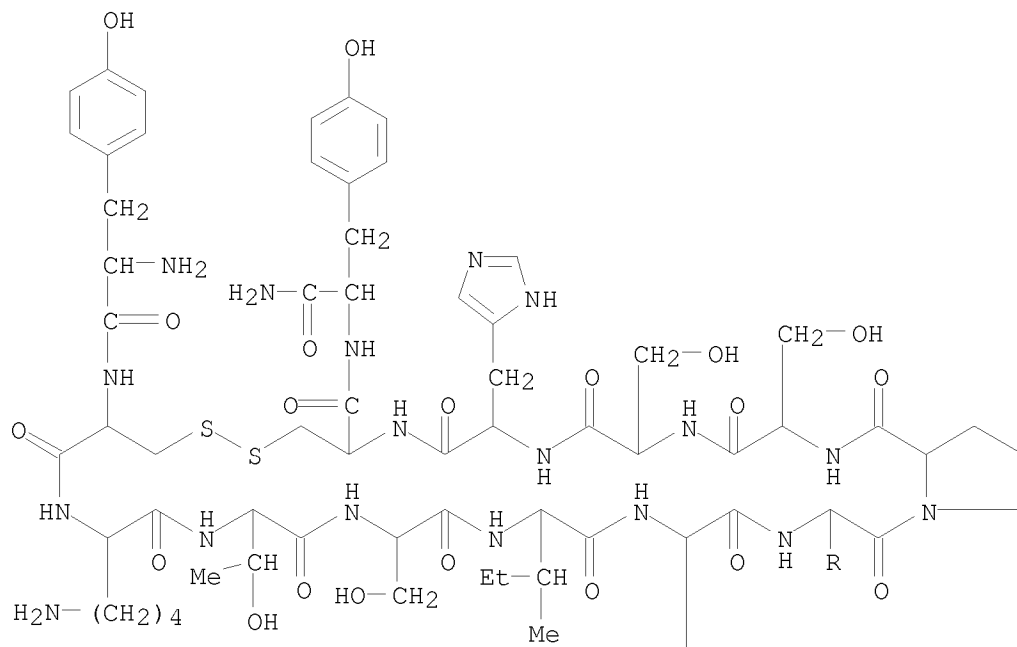
Absolute stereochemistry.



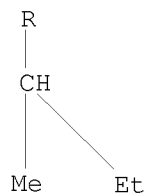
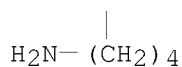


RN 325124-66-1 CAPLUS  
 CN L-Tyrosinamide, L-tyrosyl-L-cysteinyl-L-lysyl-L-threonyl-L-seryl-L-isoleucyl-L-lysyl-L-isoleucyl-L-prolyl-L-seryl-L-seryl-L-histidyl-L-cysteinyl-, cyclic (2→13)-disulfide (9CI) (CA INDEX NAME)

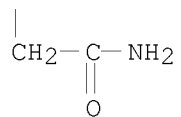
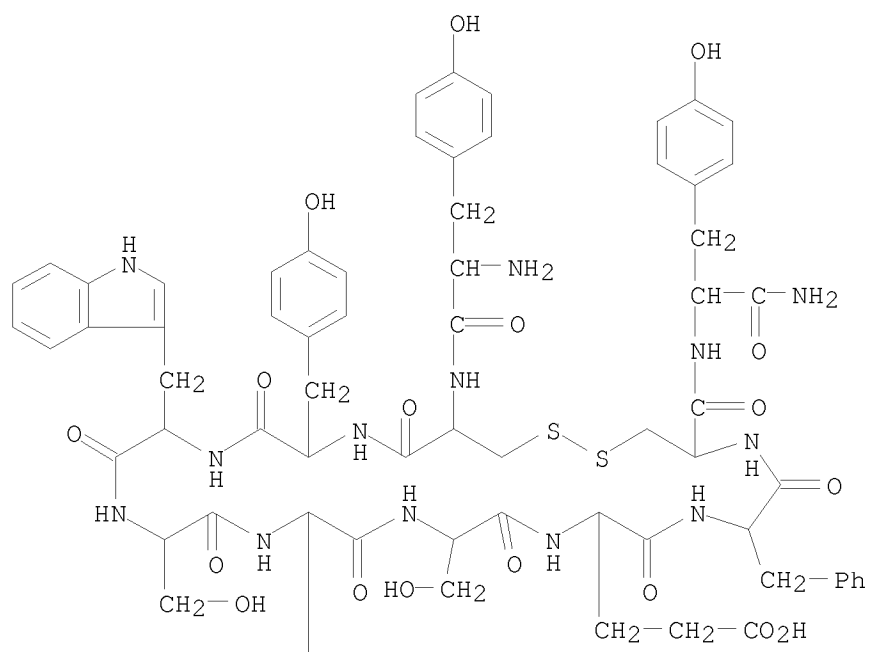
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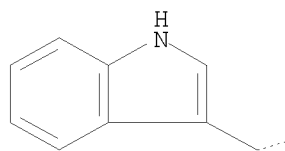
RN 325124-67-2 CAPLUS  
 CN L-Tyrosinamide, L-tyrosyl-L-cysteinyl-L-tyrosyl-L-tryptophyl-L-seryl-L-asparaginyl-L-seryl-L-α-glutamyl-L-phenylalanyl-L-cysteinyl-, cyclic (2→10)-disulfide (9CI) (CA INDEX NAME)



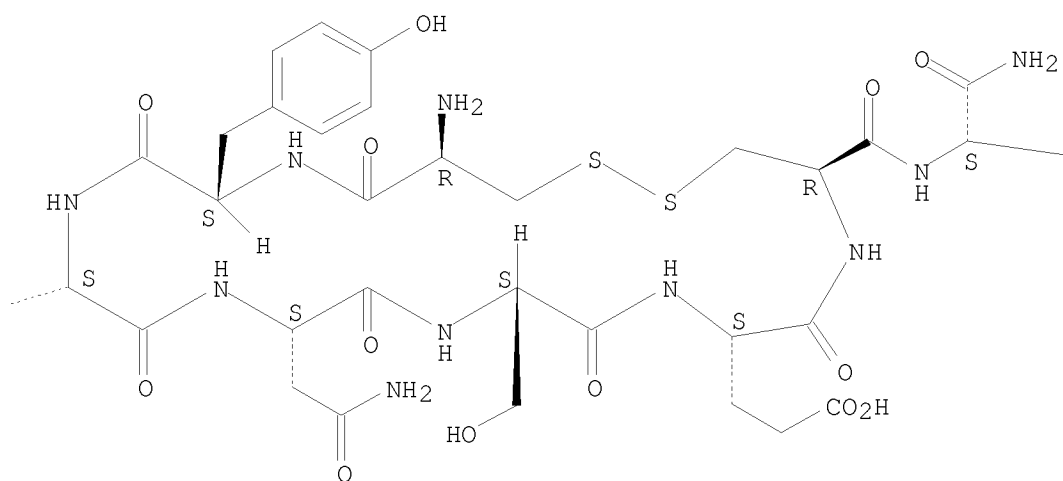
RN 325124-68-3 CAPLUS

CN L-Tyrosinamide, L-cysteinyl-L-tyrosyl-L-tryptophyl-L-asparaginyl-L-seryl-L- $\alpha$ -glutamyl-L-cysteinyl-, cyclic (1 $\rightarrow$ 7)-disulfide (9CI) (CA INDEX NAME)

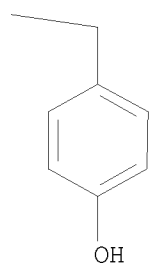
Absolute stereochemistry.



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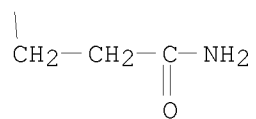
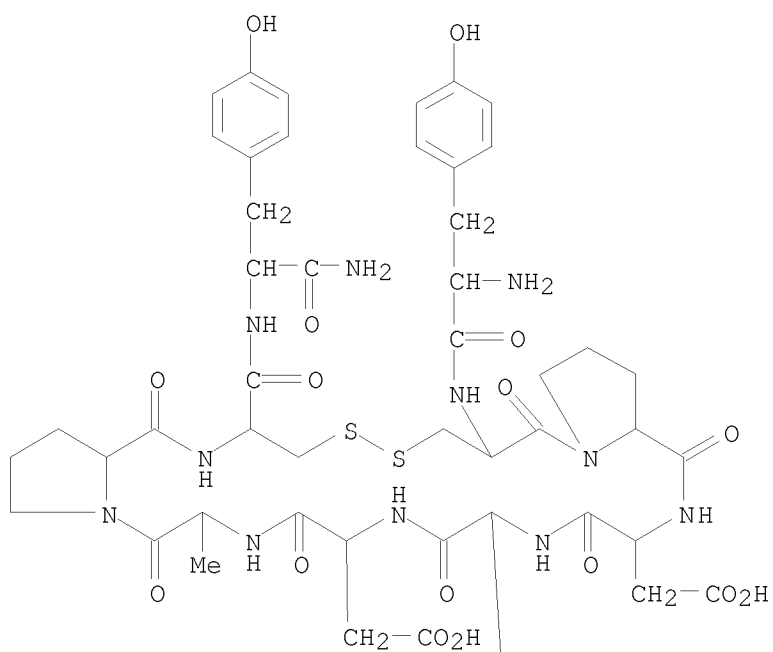


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RN 325124-69-4 CAPLUS  
 CN L-Tyrosinamide, L-tyrosyl-L-cysteinyl-L-prolyl-L- $\alpha$ -aspartyl-L-glutaminyll-L- $\alpha$ -aspartyl-L-alanyl-L-prolyl-L-cysteinyl-, cyclic (2 $\rightarrow$ 9)-disulfide (9CI) (CA INDEX NAME)



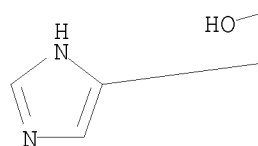


RN 325124-70-7 CAPLUS

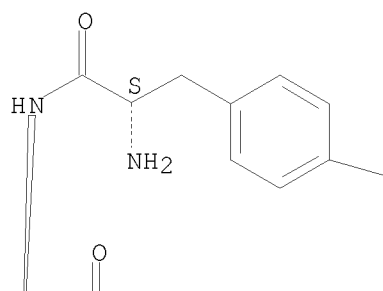
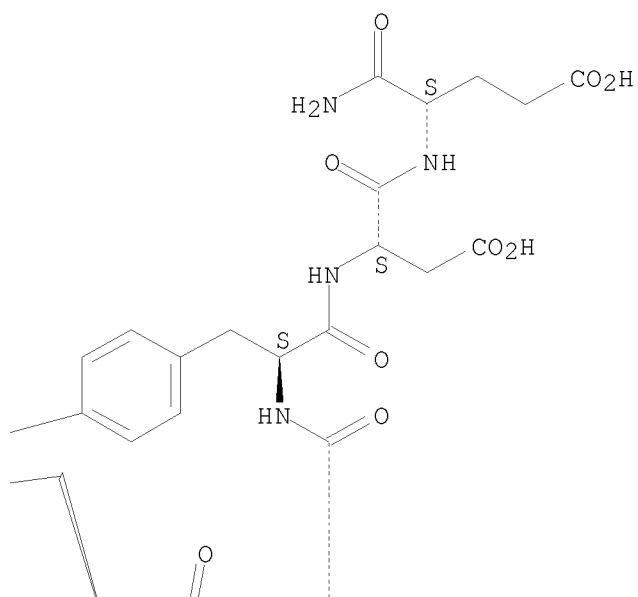
CN L- $\alpha$ -Glutamine, L-tyrosyl-L-cysteinyl-L-prolyl-L- $\alpha$ -aspartyl-L-seryl-L-tryptophyl-L-histidyl-L-cysteinyl-L-tyrosyl-L- $\alpha$ -aspartyl-, cyclic (2 $\rightarrow$ 8)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



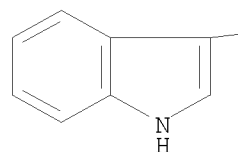
PAGE 1-B



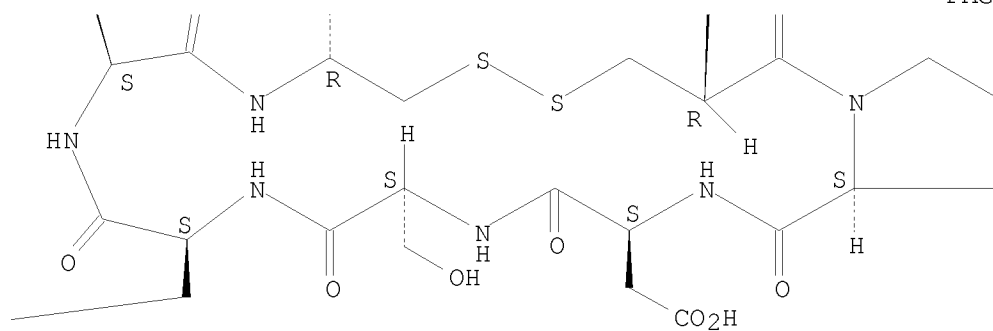
PAGE 1-C



PAGE 2-A



PAGE 2-B

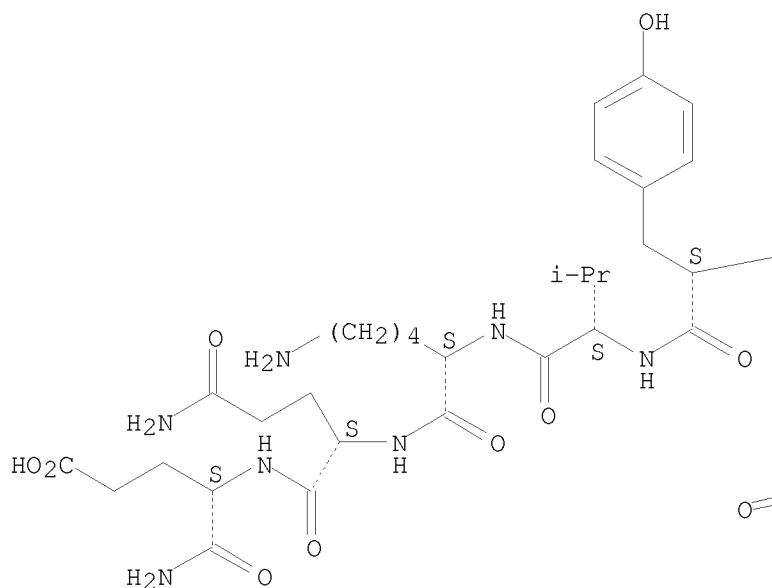


RN 325124-71-8 CAPLUS  
CN L- $\alpha$ -Glutamine, L-tyrosyl-L-cysteinyl-L-seryl-L-lysyl-L- $\alpha$ -

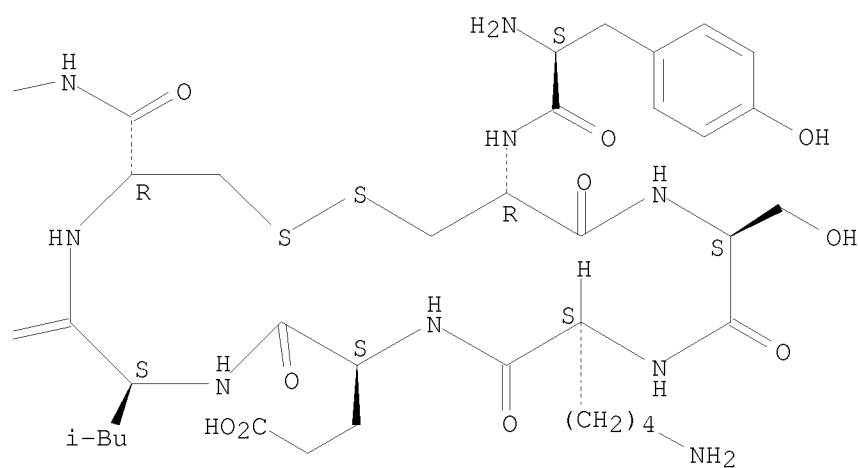
glutamyl-L-leucyl-L-cysteinyl-L-tyrosyl-L-valyl-L-lysyl-L-glutaminyl-,  
cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

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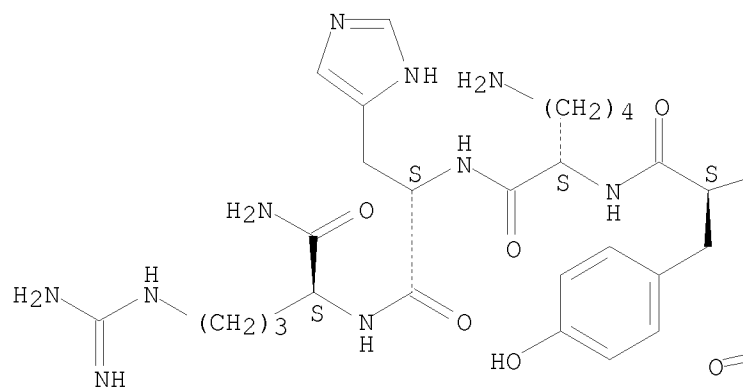


RN 325124-72-9 CAPLUS

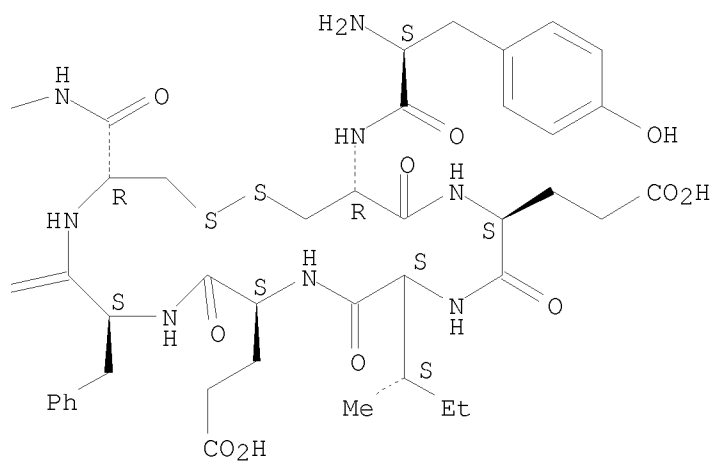
CN L-Argininamide, L-tyrosyl-L-cysteinyl-L- $\alpha$ -glutamyl-L-isoleucyl-L- $\alpha$ -glutamyl-L-phenylalanyl-L-cysteinyl-L-tyrosyl-L-lysyl-L-histidyl-,  
cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

PAGE 1-A



PAGE 1-B

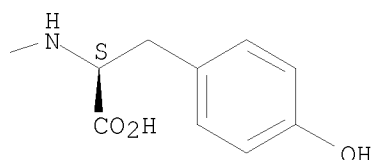


RN 325124-73-0 CAPLUS

CN L-Tyrosine, L-tyrosyl-L-cysteinyl-L-seryl-L-arginyl-L-serylglycyl-L-histidyl-L-seryl-L-cysteinyl-, cyclic (2→9)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.

NC(=O)C(=O)O



RN 325124-74-1 CAPLUS

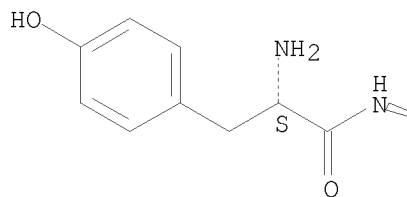
CN L-Tyrosine, L-tyrosyl-L-cysteinyl-L-arginyl-L-phenylalanyl-L-glutaminyl-L- $\alpha$ -glutamyl-L- $\alpha$ -glutamyl-L-isoleucyl-L-lysyl-L- $\alpha$ -glutamyl-L-asparaginyl-L-threonyl-L-lysyl-L-asparaginyl-L- $\alpha$ -aspartyl-L-lysyl-L-glutaminyl-L-cysteinyl-, cyclic (2 $\rightarrow$ 18)-disulfide (9CI) (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

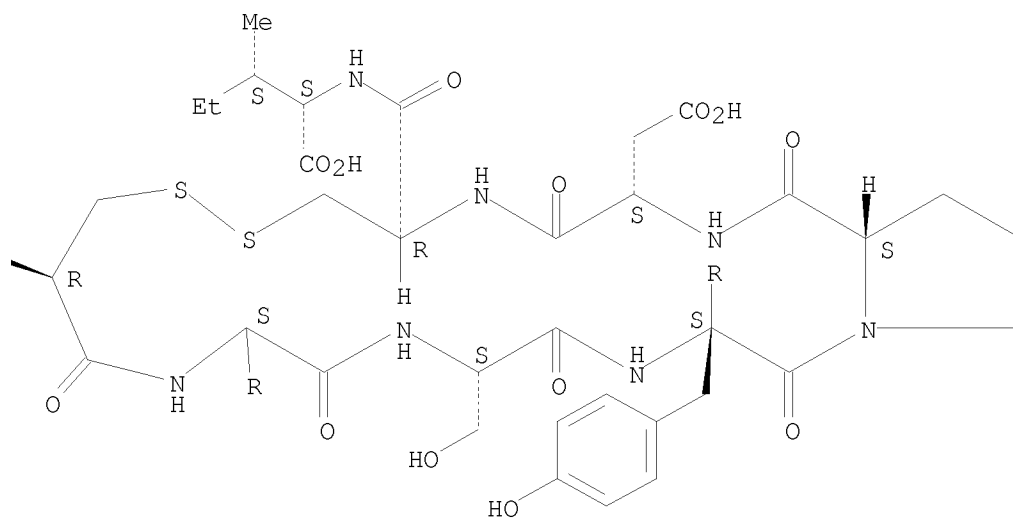
RN 325124-75-2 CAPLUS

CN L-Isoleucine, L-tyrosyl-L-cysteinyl-L-threonyl-L-seryl-L-tyrosyl-L-prolyl-L- $\alpha$ -aspartyl-L-cysteinyl-, cyclic (2 $\rightarrow$ 8)-disulfide (9CI) (CA INDEX NAME)

Absolute stereochemistry.



PAGE 1-B



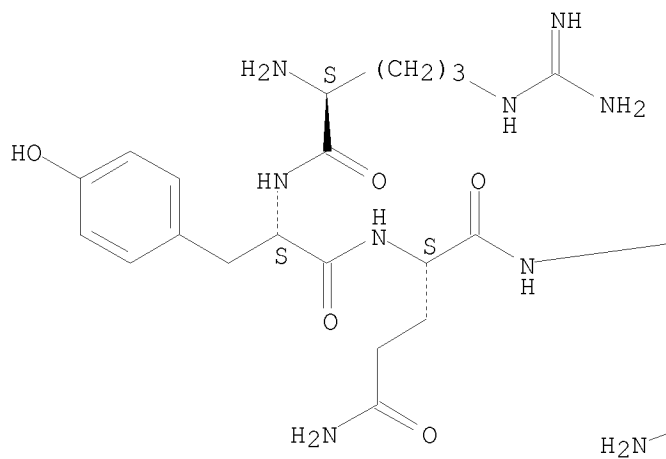
PAGE 2-A



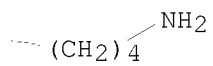
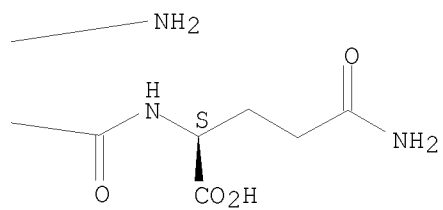
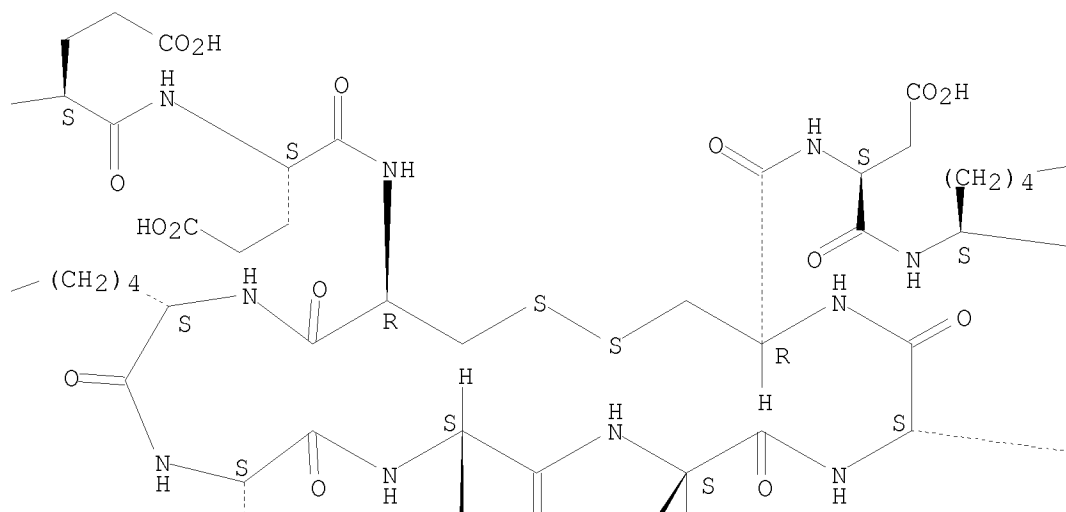
RN 325124-76-3 CAPLUS  
 CN L-Glutamine, L-arginyl-L-tyrosyl-L-glutaminyl-L- $\alpha$ -glutamyl-L- $\alpha$ -glutamyl-L-cysteinyl-L-lysyl-L- $\alpha$ -glutamyl-L-asparaginyl-L-threonyl-L-lysyl-L-cysteinyl-L- $\alpha$ -aspartyl-L-lysyl-, cyclic (6 $\rightarrow$ 12)-disulfide (9CI) (CA INDEX NAME)

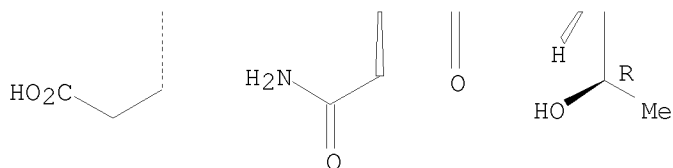
Absolute stereochemistry.

PAGE 1-A







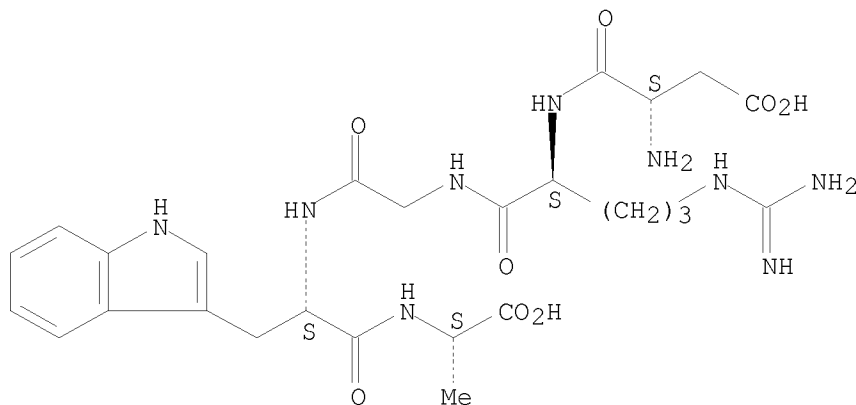


IT 207621-35-0, TRANCE  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (methods of inhibiting osteoclast activity using TRANCE/  
 RANK inhibitors and application to prevention of bone  
 loss and treatment of osteoporosis)  
 RN 207621-35-0 CAPLUS  
 CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

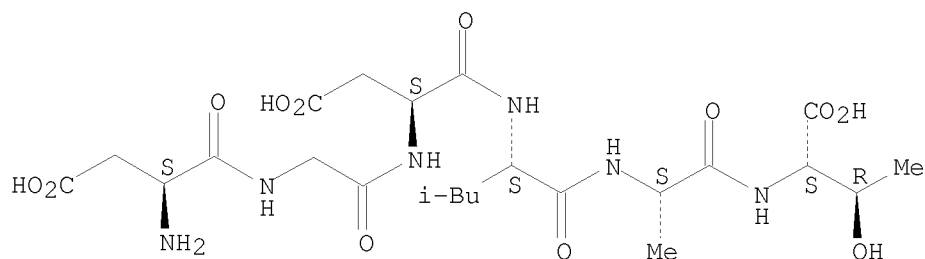
IT 325684-13-7 325684-14-8 325684-15-9  
 325684-16-0 325684-17-1 325684-18-2  
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 325684-22-8 325684-23-9 325684-24-0  
 325684-25-1 325684-26-2 325684-27-3  
 325684-28-4 325684-29-5 325684-30-8  
 RL: PRP (Properties)  
 (unclaimed sequence; methods of inhibiting osteoclastogenesis and the  
 activity of osteoclasts with TRANCE/RANK  
 inhibitors)  
 RN 325684-13-7 CAPLUS  
 CN L-Alanine, L- $\alpha$ -aspartyl-L-arginylglycyl-L-tryptophyl- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.



RN 325684-14-8 CAPLUS  
 CN L-Threonine, L- $\alpha$ -aspartylglycyl-L- $\alpha$ -aspartyl-L-leucyl-L-alanyl-  
 (9CI) (CA INDEX NAME)

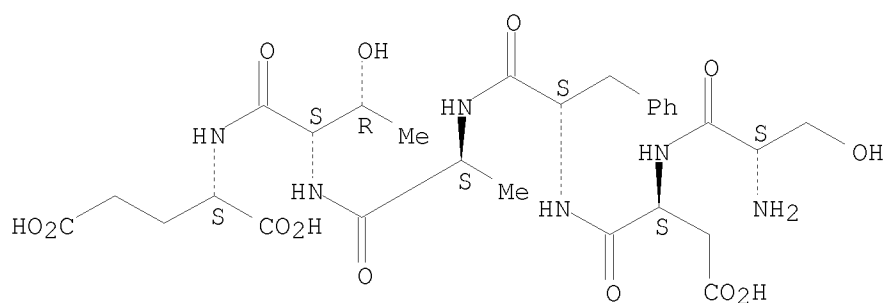
Absolute stereochemistry.



RN 325684-15-9 CAPLUS

CN L-Glutamic acid, L-seryl-L- $\alpha$ -aspartyl-L-phenylalanyl-L-alanyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

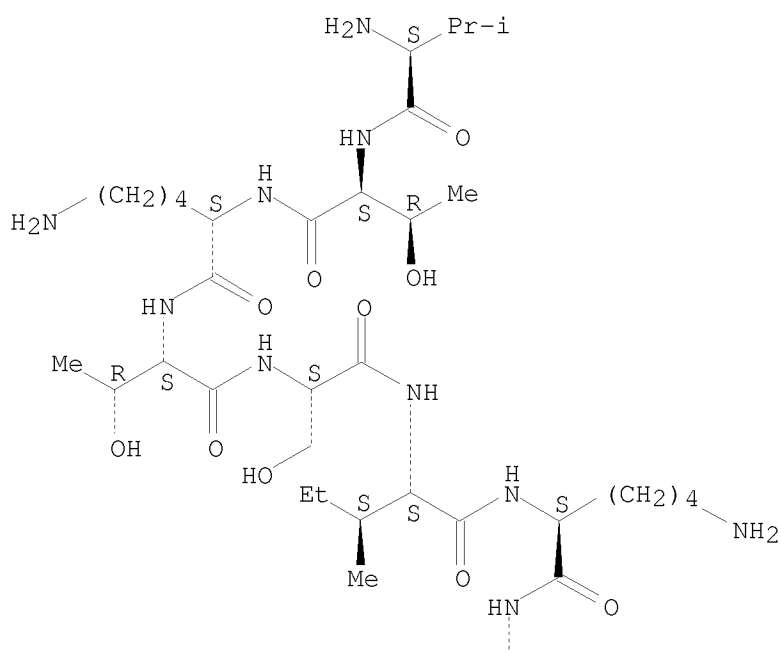


RN 325684-16-0 CAPLUS

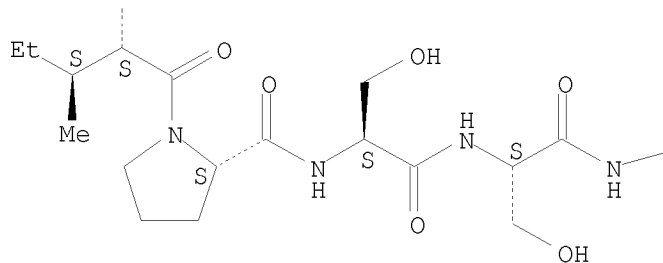
CN L-Histidine, L-valyl-L-threonyl-L-lysyl-L-threonyl-L-seryl-L-isoleucyl-L-lysyl-L-isoleucyl-L-prolyl-L-seryl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

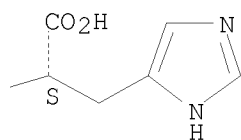
PAGE 1-A



PAGE 2-A



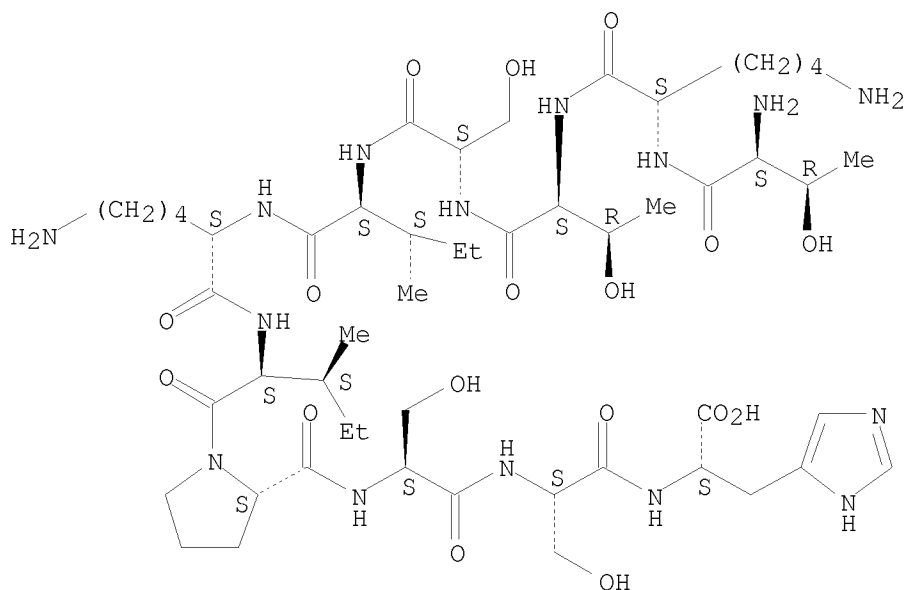
PAGE 2-B



RN 325684-17-1 CAPLUS

CN L-Histidine, L-threonyl-L-lysyl-L-threonyl-L-seryl-L-isoleucyl-L-lysyl-L-isoleucyl-L-prolyl-L-seryl-L-seryl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

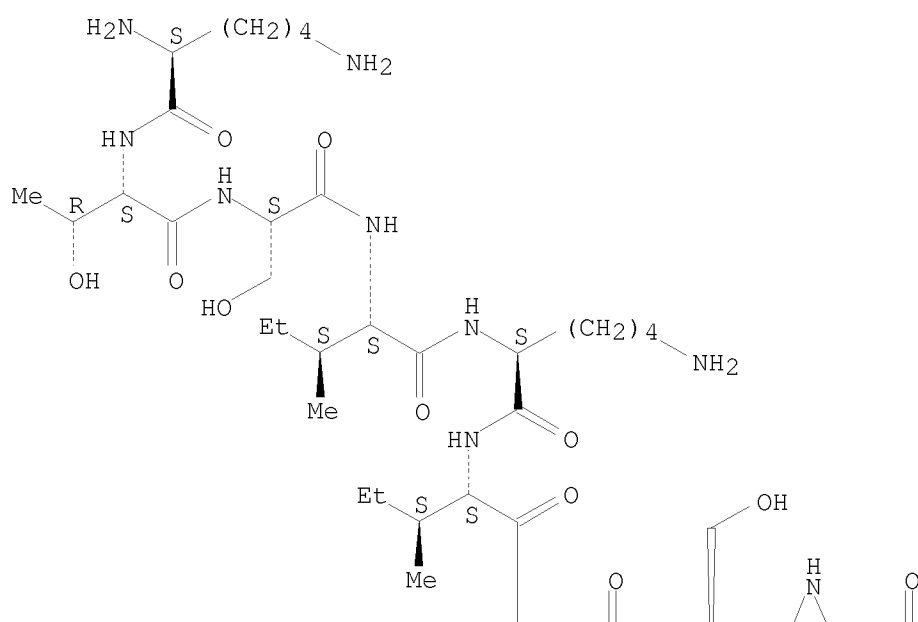


RN 325684-18-2 CAPLUS

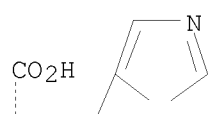
CN L-Histidine, L-lysyl-L-threonyl-L-seryl-L-isoleucyl-L-lysyl-L-isoleucyl-L-prolyl-L-seryl-L-seryl- (9CI) (CA INDEX NAME)

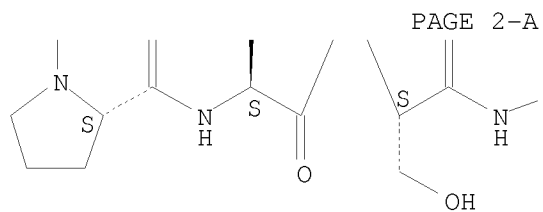
Absolute stereochemistry.

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PAGE 1-B



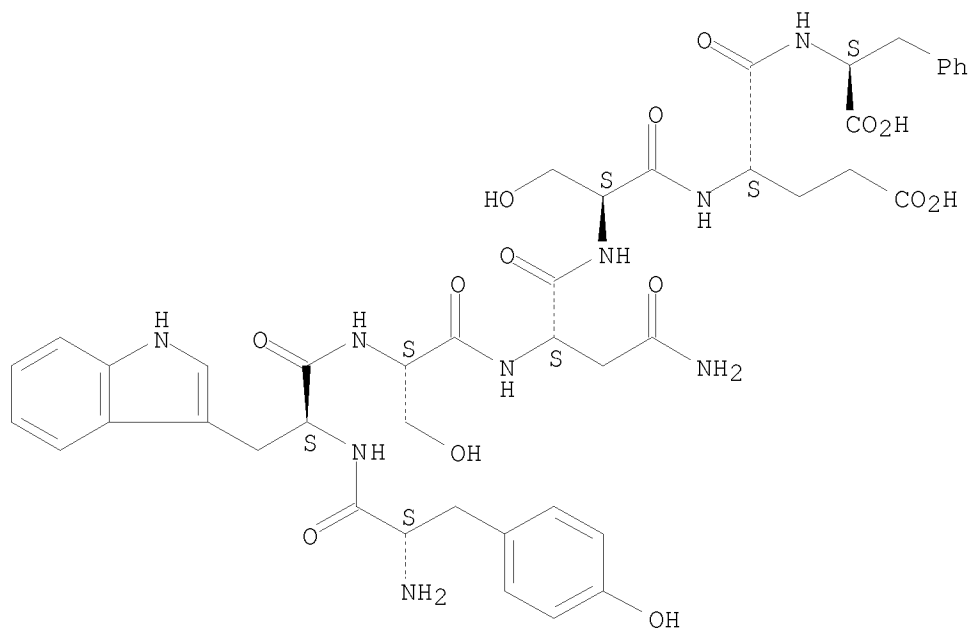


PAGE 2-B

RN 325684-19-3 CAPLUS

CN L-Phenylalanine, L-tyrosyl-L-tryptophyl-L-seryl-L-asparaginyl-L-seryl-L- $\alpha$ -glutamyl- (9CI) (CA INDEX NAME)

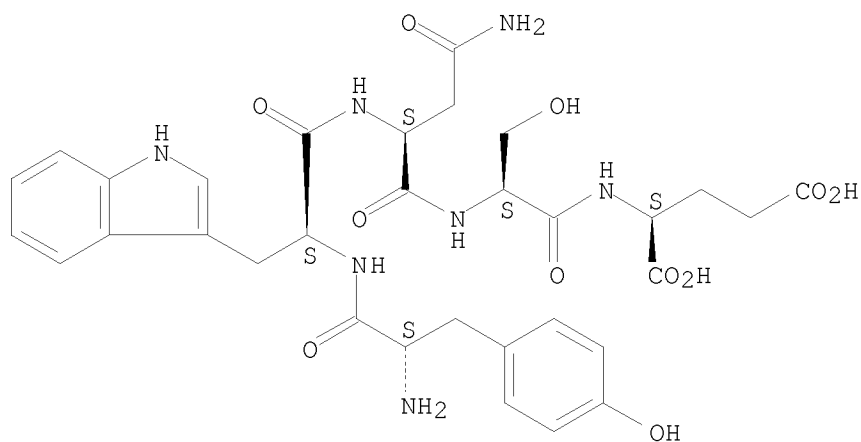
Absolute stereochemistry.



RN 325684-20-6 CAPLUS

CN L-Glutamic acid, L-tyrosyl-L-tryptophyl-L-asparaginyl-L-seryl- (9CI) (CA INDEX NAME)

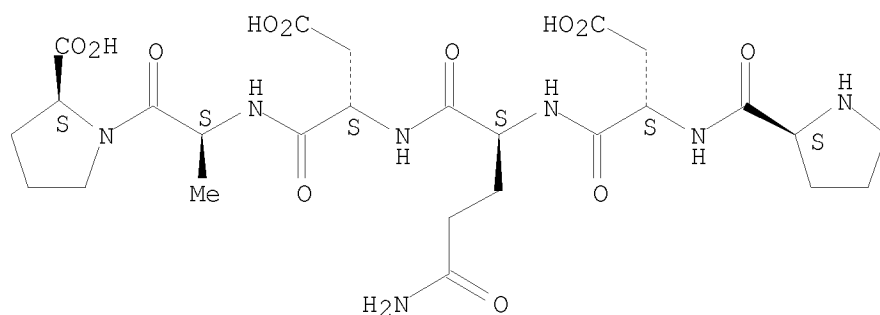
Absolute stereochemistry.



RN 325684-21-7 CAPLUS

CN L-Proline, L-prolyl-L- $\alpha$ -aspartyl-L-glutaminyl-L- $\alpha$ -aspartyl-L-alanyl- (9CI) (CA INDEX NAME)

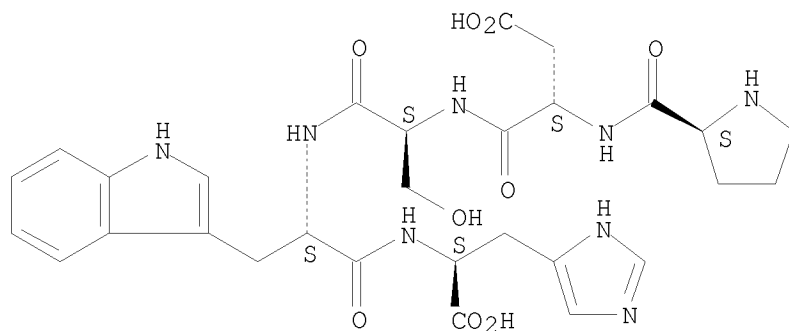
Absolute stereochemistry.



RN 325684-22-8 CAPLUS

CN L-Histidine, L-prolyl-L- $\alpha$ -aspartyl-L-seryl-L-tryptophyl- (9CI) (CA INDEX NAME)

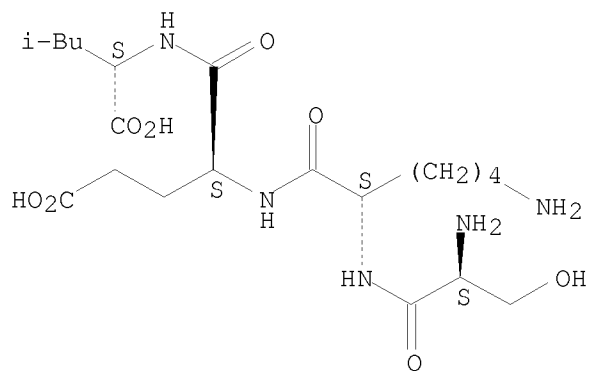
Absolute stereochemistry.



RN 325684-23-9 CAPLUS

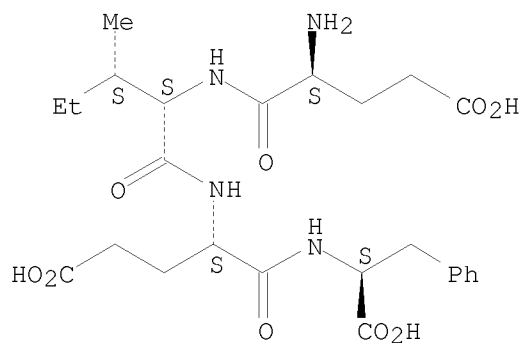
CN L-Leucine, L-seryl-L-lysyl-L- $\alpha$ -glutamyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



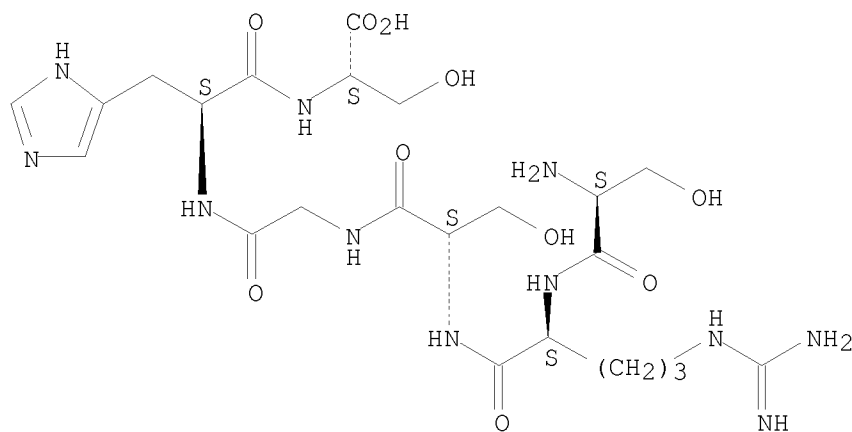
RN 325684-24-0 CAPLUS  
 CN L-Phenylalanine, L- $\alpha$ -glutamyl-L-isoleucyl-L- $\alpha$ -glutamyl- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



RN 325684-25-1 CAPLUS  
 CN L-Serine, L-seryl-L-arginyl-L-serylglycyl-L-histidyl- (9CI) (CA INDEX  
 NAME)

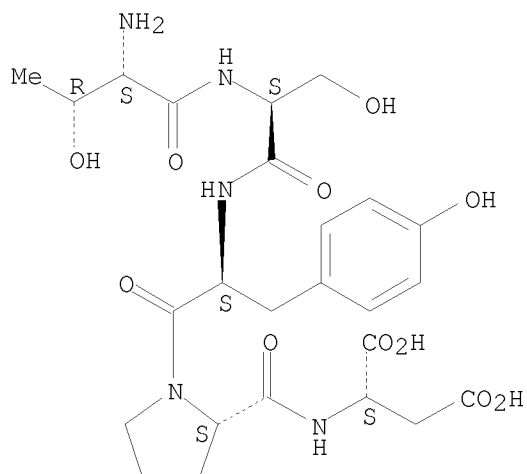
Absolute stereochemistry.



RN 325684-26-2 CAPLUS  
 CN L-Aspartic acid, L-threonyl-L-seryl-L-tyrosyl-L-prolyl- (9CI) (CA INDEX  
 NAME)

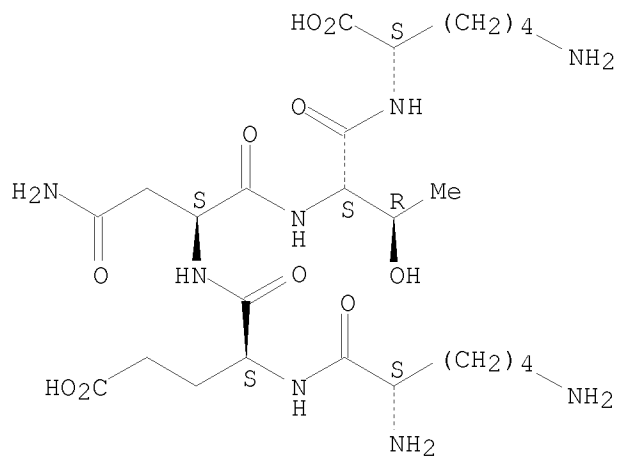


Absolute stereochemistry.



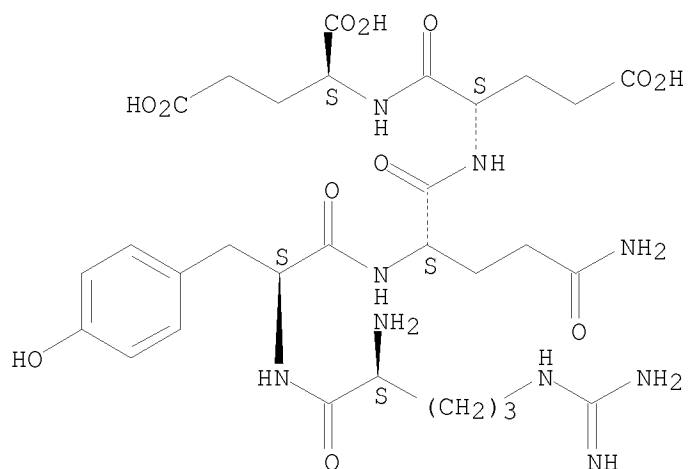
RN 325684-27-3 CAPLUS  
 CN L-Lysine, L-lysyl-L- $\alpha$ -glutamyl-L-asparaginyl-L-threonyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 325684-28-4 CAPLUS  
 CN L-Glutamic acid, L-arginyl-L-tyrosyl-L-glutaminyl-L- $\alpha$ -glutamyl- (9CI) (CA INDEX NAME)

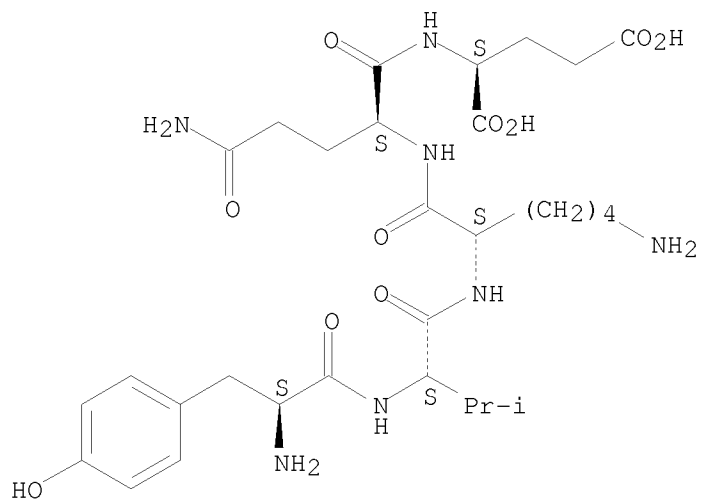
Absolute stereochemistry.



RN 325684-29-5 CAPLUS

CN L-Glutamic acid, L-tyrosyl-L-valyl-L-lysyl-L-glutaminyll- (9CI) (CA INDEX NAME)

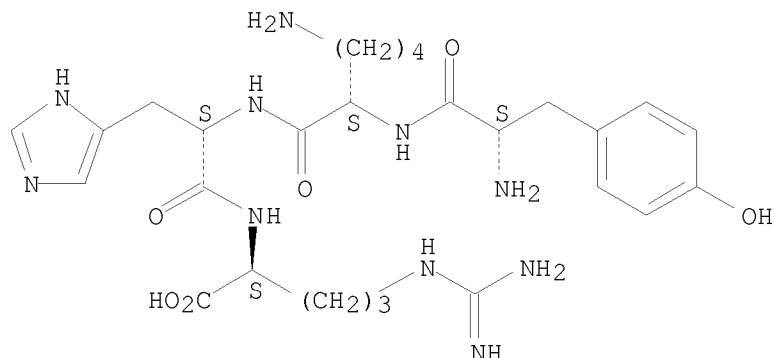
Absolute stereochemistry.



RN 325684-30-8 CAPLUS

CN L-Arginine, L-tyrosyl-L-lysyl-L-histidyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB Methods of inhibiting osteoclastogenesis and the activity of osteoclasts are disclosed. Methods of treating patients who have diseases characterized bone loss are disclosed. According to the methods, an amount of a TRANCE/RANK inhibitor effective to inhibit osteoclastogenesis is administered to the patient. Pharmaceutical compns. which comprise TRANCE/RANK inhibitor in an amount effective to inhibit osteoclastogenesis. Methods of modulating dendritic cell maturation, T cell proliferation, and/or CD40 receptor systems in an individual are disclosed. The methods comprise the step of administering to the individual an amount of a TRANCE/RANK inhibitor effective to modulating dendritic cell maturation, T cell proliferation, and/or CD40 receptor systems.

ACCESSION NUMBER: 2001:100972 CAPLUS  
DOCUMENT NUMBER: 134:157587  
TITLE: Methods of inhibiting osteoclastogenesis and the activity of osteoclasts with TRANCE/RANK inhibitors  
INVENTOR(S): Murali, Ramachandran; Greene, Mark I.; Kinosaki, Masahiko  
PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA  
SOURCE: PCT Int. Appl., 81 pp.  
CODEN: PIXXD2  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
FAMILY ACC. NUM. COUNT: 1  
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001008677	A1	20010208	WO 2000-US20502	20000727
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2380007	A1	20010208	CA 2000-2380007	20000728
EP 1207873	A1	20020529	EP 2000-950797	20000728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
JP 2003505503	T	20030212	JP 2001-513407	20000728
US 6673771	B1	20040106	US 2000-628665	20000728
AU 778190	B2	20041118	AU 2000-63846	20000728
US 20050080133	A1	20050414	US 2003-625073	20030722
AU 2005200650	A1	20050310	AU 2005-200650	20050214
AU 2005200650	B2	20071115		
AU 2008200757	A1	20080313	AU 2008-200757	20080215
PRIORITY APPLN. INFO.:			US 1999-146094P	P 19990728

WO 2000-US20502 W 20000727  
US 2000-628665 A3 20000728  
AU 2005-200650 A3 20050214

OTHER SOURCE(S): MARPAT 134:157587  
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 9 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 205944-50-9, Osteoprotegerin 207621-35-0, Osteoclast  
differentiation factor  
RL: BOC (Biological occurrence); BSU (Biological study, unclassified);  
BIOL (Biological study); OCCU (Occurrence)  
(osteoclast differentiation factor, RANK, osteoprotegrin,  
TRAIL and ODF receptors expression by stromal elements of giant cell  
tumors)

RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 207621-35-0 CAPLUS  
CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

AB The mechanisms by which primary tumors of the bone cause  
bone destruction have not been elucidated. Unlike most other  
lytic bone tumors, osteoclastomas, otherwise known as giant cell  
tumors (GCT), contain osteoclast-like cells within the tumor stroma. A  
new member of the TNF-ligand superfamily member, osteoclast  
differentiation factor (ODF/OPGL/RANKL/TRANCE), was recently  
identified. ODF was shown to directly stimulate osteoclastogenesis, in  
the presence of M-CSF. In this study, the expression of ODF was examined in  
a number of tumor samples associated with bone lysis in vivo. In  
addition, we investigated expression of the ODF receptor on osteoclast  
precursors, RANK, as well as the ODF inhibitor  
osteoprotegerin (OPG), and another TNF-ligand superfamily member, TRAIL,  
previously shown to abrogate the inhibitory effects of OPG. We report  
here the novel finding that GCT stromal cells contain abundant ODF mRNA,  
whereas the giant cell population exclusively expresses RANK  
mRNA. These results are consistent with the osteoclast-mediated  
bone destruction by these tumors. We also report the expression  
of OPG and TRAIL mRNA in GCT samples. A comparison with other lytic and  
nonlytic tumors of bone showed that GCT express more ODF and  
TRAIL mRNA relative to OPG mRNA. In addition, GCT were found to express a  
number of cytokines previously reported to play central roles in  
osteoclastogenesis, namely, IL-1, -6, -11, -17, as well as TNF- $\alpha$ .  
Importantly, GCT were also found to express high levels of M-CSF mRNA, a  
cytokine shown to be an essential cofactor of ODF, and a survival factor  
for mature and developing osteoclasts. Furthermore, expression of these  
mols. by stromal cells isolated from GCT continued in vitro. Thus GCT  
constitutively express all of the signals that are currently understood to  
be necessary for the differentiation of osteoclasts from precursor cells.

ACCESSION NUMBER: 2000:251544 CAPLUS

DOCUMENT NUMBER: 133:148374

TITLE: Expression of osteoclast differentiation signals by  
stromal elements of giant cell tumors

AUTHOR(S): Atkins, Gerald J.; Haynes, David R.; Graves, Stephen  
E.; Evdokiou, Andreas; Hay, Shelley; Bouralexis,  
Stelios; Findlay, David M.

CORPORATE SOURCE: Department of Orthopaedics and Trauma, University of  
Adelaide, Adelaide, 5000, Australia

SOURCE: Journal of Bone and Mineral Research (2000), 15(4),  
640-649

PUBLISHER: CODEN: JBMREJ; ISSN: 0884-0431  
DOCUMENT TYPE: American Society for Bone and Mineral Research  
LANGUAGE: Journal  
REFERENCE COUNT: English  
24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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FILE 'CAPLUS' ENTERED AT 07:41:46 ON 29 JUL 2008

L1 0 S 20050080133  
L2 0 S US 20050080133 A1  
L3 0 S US 20050080133  
L4 0 S US20050080133  
L5 1 S US20050080133/PN  
SEL RN

FILE 'REGISTRY' ENTERED AT 07:58:33 ON 29 JUL 2008

L6 97 S E1-97

FILE 'CAPLUS' ENTERED AT 07:59:10 ON 29 JUL 2008

L7 9880 S L6  
L8 2598 S L6 AND BONE  
L9 0 S L8 AND TRANCE/RANK  
L10 9 S L8 AND TRANCE AND RANK AND INHIBITOR

=> s 18 and pd<1999  
19245022 PD<1999  
(PD<19990000)

L11 46 L8 AND PD<1999

=> d l11 1-46 hitstr ibib abs

L11 ANSWER 1 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 207621-35-0, RANK ligand

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(mRNA, antisense oligonucleotide to; administering parathyroid hormone  
for increasing RANKL in mouse model for osteoporosis and its use in  
drug screening)

RN 207621-35-0 CAPLUS

CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 2005:238769 CAPLUS

DOCUMENT NUMBER: 142:291451

TITLE: Administering parathyroid hormone for increasing RANKL  
in mouse model for osteoporosis and its use in drug  
screening

INVENTOR(S): Gregory, Susan

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 101 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 326

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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US 20050060764	A1	20050317	US 2003-667236	20030917
AU 9726244	A	19971106	AU 1997-26244	19970624 <--
AU 713740	B2	19991209		
US 6232463	B1	20010515	US 1998-128508	19980804
US 20050261228	A1	20051124	US 2005-89191	20050323

PRIORITY APPLN. INFO.:

US 1992-954185	B2	19920929
AU 1993-38025	A3	19930225
WO 1993-US9297	W	19930929
US 1995-403888	A1	19950612
US 1997-948151	A1	19971009
US 1998-205144	A1	19981203
US 1998-205204	A1	19981203
US 1999-299058	B2	19990423
WO 1999-US13624	A1	19990616
US 1999-392580	A1	19990909
WO 1999-US22083	W	19990923
WO 2000-US583	W	20000111
US 2001-851520	A2	20010507
US 2001-857278	B2	20010924
US 2001-857299	B2	20011004
US 2002-38335	A2	20020102
WO 2002-US13871	W	20020501
US 2002-388074P	P	20020611
US 2002-388100P	P	20020611
US 2002-388118P	P	20020611
US 2002-188883	A2	20020702
US 2002-197290	A1	20020716
US 2002-70789	B2	20020806
WO 2003-US18258	W	20030610
WO 2003-US18312	W	20030610
WO 2003-US18320	W	20030610
US 2003-464158	A2	20030618
US 2003-667236	A2	20030917
US 2003-476960	A2	20031105
US 2004-512739	A2	20041027
US 2004-515545	A2	20041123
US 2004-515546	A2	20041123
US 2005-48271	A2	20050201

AB A mouse model for short-term bone resorption by infusion or parathyroid hormone (PTH), PTH fragments, PTH analogs, parathyroid hormone-related protein (PTHrP), PTHrP fragments, or PTRrP analogs is provided. In particular, the present invention relates to administering parathyroid hormone for increasing RANKL mRNA expression and serum calcium concentration in mouse model for osteoporosis. The mouse os exposed to to 0.5-8 g of parathyroid hormone or analog per 100 g of bodyweight. The mouse model can be used to screen for therapeutic agents for osteoporosis.

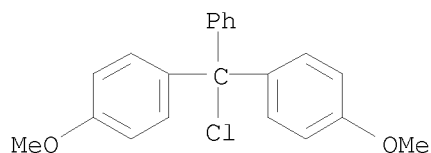
L11 ANSWER 2 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 40615-36-9

RL: RCT (Reactant); RACT (Reactant or reagent)  
(antisense modulation of cell division cycle 2 protein kinase expression)

RN 40615-36-9 CAPLUS

CN Benzene, 1,1'-(chlorophenylmethylene)bis[4-methoxy- (CA INDEX NAME)



ACCESSION NUMBER: 2004:20324 CAPLUS  
 DOCUMENT NUMBER: 140:105242  
 TITLE: Antisense modulation of cell division cycle 2 expression  
 INVENTOR(S): Dean, Nicholas M.; Freier, Susan M.  
 PATENT ASSIGNEE(S): Isis Pharmaceuticals Inc., USA  
 SOURCE: U.S. Pat. Appl. Publ., 61 pp.  
 CODEN: USXXCO  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 326  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20040006029	A1	20040108	US 2002-189266	20020702
AU 9726244	A	19971106	AU 1997-26244	19970624 <--
AU 713740	B2	19991209		
US 6232463	B1	20010515	US 1998-128508	19980804
US 20050215504	A1	20050929	US 2004-14360	20041216
PRIORITY APPLN. INFO.:			AU 1993-38025	A3 19930225
			US 1997-948151	A1 19971009
			US 2002-114683	B2 20020402
			US 2002-131544	B2 20020423
			US 2002-144140	B2 20020510
			US 2002-146860	B2 20020515
			US 2002-160497	B2 20020530
			US 2002-159942	A2 20020531
			US 2002-161983	B2 20020531
			US 2002-161996	B2 20020604
			US 2002-173718	B2 20020617
			US 2002-174014	A2 20020617
			US 2002-174175	A2 20020617
			US 2002-174319	B2 20020617
			US 2002-174460	A2 20020617
			US 2002-176277	B2 20020618
			US 2002-185057	B2 20020628
			US 2002-188779	A2 20020702
			US 2002-189266	B2 20020702
			US 2002-189267	B2 20020702
			US 2002-200293	A2 20020718
			US 2002-199675	B2 20020719
			US 2002-211179	B2 20020801
			US 2002-215821	B2 20020809
			US 2002-317500	A2 20021211

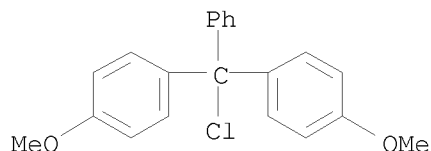
AB Antisense compds., compns. and methods are provided for modulating the expression of cell division cycle 2. The compns. comprise antisense compds., particularly antisense oligonucleotides, targeted to nucleic acids encoding cell division cycle 2. Methods of using these compds. for modulation of cell division cycle 2 expression and for treatment of diseases associated with expression of cell division cycle 2 are provided.

RL: RCT (Reactant); RACT (Reactant or reagent)

(antisense modulation of IL-1 receptor-associated kinase-1 expression and therapeutic use thereof)

RN 40615-36-9 CAPLUS

CN Benzene, 1,1'-(chlorophenylmethylene)bis[4-methoxy- (CA INDEX NAME)



ACCESSION NUMBER: 2003:971629 CAPLUS

DOCUMENT NUMBER: 140:23216

TITLE: Antisense modulation of IL-1 receptor-associated kinase-1 expression and therapeutic use thereof

INVENTOR(S): Baker, Brenda F.; Freier, Susan M.; Dobie, Kenneth W.

PATENT ASSIGNEE(S): Isis Pharmaceuticals Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 66 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 326

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20030228690	A1	20031211	US 2002-167034	20020610
AU 9726244	A	19971106	AU 1997-26244	19970624 <--
AU 713740	B2	19991209		
US 6232463	B1	20010515	US 1998-128508	19980804
WO 2003104458	A1	20031218	WO 2003-US18003	20030609
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 2003237469	A1	20031222	AU 2003-237469	20030609
US 20050153925	A1	20050714	US 2004-13608	20041216
PRIORITY APPLN. INFO.:	AU 1993-38025 A3 19930225			
	US 1997-948151 A1 19971009			
	US 2002-154708 B2 20020522			
	US 2002-159834 B2 20020531			
	US 2002-167034 A 20020610			
	US 2002-175627 A2 20020618			
	US 2002-186157 A2 20020628			
	US 2002-189268 A2 20020702			
	US 2002-189406 A2 20020703			
	US 2002-199199 A2 20020718			
	US 2002-199674 A2 20020719			
	US 2002-210802 A2 20020731			
	US 2002-292849 A2 20021111			
	US 2002-293863 A2 20021111			
	US 2002-295471 A2 20021116			
	US 2002-298123 A2 20021116			



US	2002-298953	A2	20021116
US	2002-298994	A2	20021116
US	2002-300642	A2	20021119
US	2002-303329	A2	20021121
US	2002-303541	A2	20021121
US	2002-303588	A2	20021122
US	2002-304019	A2	20021123
US	2002-304113	A2	20021123
US	2002-304116	A2	20021123
US	2002-304125	A2	20021123
US	2002-315765	A2	20021209
US	2002-317883	A2	20021211
US	2002-318819	A2	20021212
US	2002-319914	A2	20021212
WO	2003-US18003	W	20030609

AB Antisense compds., compns. and methods are provided for modulating the expression of IL-1 receptor-associated kinase-1. The compns. comprise antisense compds., particularly antisense oligonucleotides, targeted to nucleic acids encoding IL-1 receptor-associated kinase-1. Thus, 20-nucleotide, phosphorothioate-linked, chimeric oligonucleotides targeting the 5'-UTR, the coding region, or the 3'-UTR of IL-1 receptor-associated kinase-1 mRNA were synthesized. These oligonucleotides contain 5-methylcytosine in place of cytosine and consist of a 10-nucleotide DNA core flanked on both sides by five 2'-O'(2-methoxyethyl)ribonucleosides. In transfected A549 cells, 57 of these antisense oligonucleotides (not specifically claimed, out of total 72) demonstrated at least 60% inhibition of IL-1 receptor-associated kinase-1 gene expression. Methods of using these compds. for modulation of IL-1 receptor-associated kinase-1 expression and for treatment of diseases associated with expression of IL-1 receptor-associated kinase-1, such as rheumatoid arthritis, are provided.

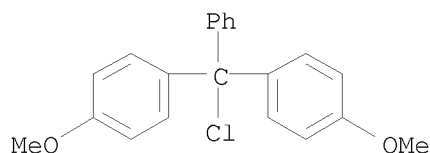
L11 ANSWER 4 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 40615-36-9

RL: RCT (Reactant); RACT (Reactant or reagent)  
(antisense modulation of estrogen receptor beta expression for treatment of cancer)

RN 40615-36-9 CAPLUS

CN Benzene, 1,1'-(chlorophenylmethylene)bis[4-methoxy- (CA INDEX NAME)



ACCESSION NUMBER: 2003:472524 CAPLUS

DOCUMENT NUMBER: 139:63308

TITLE: Antisense modulation of estrogen receptor beta expression for treatment of cancer

INVENTOR(S): Dobie, Kenneth W.; Roach, Mark P.; Koller, Erich

PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 160 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 326

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003050133	A1	20030619	WO 2002-US39200	20021206
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 9726244	A	19971106	AU 1997-26244	19970624 <--
AU 713740	B2	19991209		
US 6232463	B1	20010515	US 1998-128508	19980804
AU 2002353076	A1	20030623	AU 2002-353076	20021206
PRIORITY APPLN. INFO.:				
			US 2001-5058	A 20011207
			AU 1993-38025	A3 19930225
			US 1997-948151	A1 19971009
			WO 2002-US39200	W 20021206

AB Antisense compds., compns. and methods are provided for modulating the expression of estrogen receptor beta. The compns. comprise antisense compds., particularly antisense oligonucleotides, targeted to nucleic acids encoding estrogen receptor beta. Methods of using these compds. for modulation of estrogen receptor beta expression and for treatment of diseases associated with expression of estrogen receptor beta are provided.

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 5 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

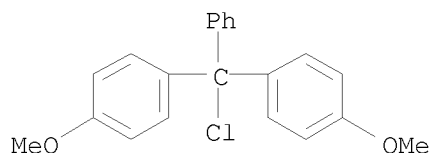
IT 40615-36-9

RL: RCT (Reactant); RACT (Reactant or reagent)

(antisense modulation of fibroblast growth factor receptor 3 (FGFR-3) expression for treatment of hyperproliferative disorders)

RN 40615-36-9 CAPLUS

CN Benzene, 1,1'-(chlorophenylmethylene)bis[4-methoxy- (CA INDEX NAME)



ACCESSION NUMBER: 2003:221814 CAPLUS

DOCUMENT NUMBER: 138:248496

TITLE: Antisense modulation of fibroblast growth factor receptor 3 (FGFR-3) expression for treatment of hyperproliferative disorders

INVENTOR(S): Monia, Brett P.; Wyatt, Jacqueline R.

PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA

SOURCE: PCT Int. Appl., 120 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

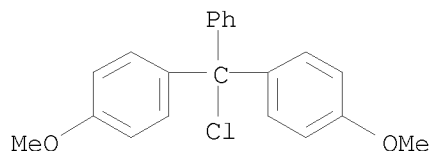
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 326

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003023004 A2 20030320 WO 2002-US28549 20020906  
 WO 2003023004 A3 20031120  
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 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,  
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,  
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,  
 UA, UG, UZ, VN, YU, ZA, ZM, ZW  
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,  
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 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF,  
 CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG  
 AU 9726244 A 19971106 AU 1997-26244 19970624 <--  
 AU 713740 B2 19991209  
 US 6232463 B1 20010515 US 1998-128508 19980804  
 US 20030087854 A1 20030508 US 2001-953047 20010910  
 AU 2002332923 A1 20030324 AU 2002-332923 20020906  
 EP 1436430 A2 20040714 EP 2002-798163 20020906  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK  
 PRIORITY APPLN. INFO.: US 2001-953047 A 20010910  
 AU 1993-38025 A3 19930225  
 US 1997-948151 A1 19971009  
 WO 2002-US28549 W 20020906  
 AB Antisense compds., compns. and methods are provided for modulating the  
 expression of fibroblast growth factor receptor 3. The compns. comprise  
 antisense compds., particularly antisense oligonucleotides, targeted to  
 nucleic acids encoding fibroblast growth factor receptor 3. Methods of  
 using these compds. for modulation of fibroblast growth factor receptor 3  
 expression and for treatment of diseases associated with expression of  
 fibroblast growth factor receptor 3 are provided.  
 L11 ANSWER 6 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
 IT 40615-36-9  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (antisense modulation of transforming growth factor beta receptor II  
 (TGFβ-II) expression for treatment of tumors)  
 RN 40615-36-9 CAPLUS  
 CN Benzene, 1,1'-(chlorophenylmethylene)bis[4-methoxy- (CA INDEX NAME)



ACCESSION NUMBER: 2003:5927 CAPLUS  
 DOCUMENT NUMBER: 138:83348  
 TITLE: Antisense modulation of transforming growth factor  
 beta receptor II expression  
 INVENTOR(S): Murray, Susan F.; Wyatt, Jacqueline R.  
 PATENT ASSIGNEE(S): Isis Pharmaceuticals, Inc., USA  
 SOURCE: PCT Int. Appl., 141 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 326  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 2003000656	A2	20030103	WO 2002-US19665	20020619
WO 2003000656	A3	20030227		
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RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
AU 9726244	A	19971106	AU 1997-26244	19970624 <--
AU 713740	B2	19991209		
US 6232463	B1	20010515	US 1998-128508	19980804
US 20030064944	A1	20030403	US 2001-888361	20010621
AU 2002316318	A1	20030108	AU 2002-316318	20020619
EP 1406915	A2	20040414	EP 2002-746611	20020619
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR			
JP 2005504522	T	20050217	JP 2003-507063	20020619
PRIORITY APPLN. INFO.:			US 2001-888361	A 20010621
			AU 1993-38025	A3 19930225
			US 1997-948151	A1 19971009
			WO 2002-US19665	W 20020619

AB Antisense compds., compns. and methods are provided for modulating the expression of Transforming growth factor beta receptor II. The compns. comprise antisense compds., particularly antisense oligonucleotides, targeted to nucleic acids encoding Transforming growth factor beta receptor II. Methods of using these compds. for modulation of Transforming growth factor beta receptor II expression and for treatment of diseases associated with expression of Transforming growth factor beta receptor II are provided. Diseases being treated with antisense oligonucleotides include lung cancer, liver cancer, bone cancer, breast cancer, cervical cancer, colon cancer, gastric cancer, pancreatic cancer, esophageal cancer and hematopoietic cancer.

L11 ANSWER 7 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9P, Osteoprotegerin

RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(gene OPG for, of human, rat and mouse; osteoprotegerin in treatment of osteoporosis and other bone diseases)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 2002:271976 CAPLUS

DOCUMENT NUMBER: 136:274360

TITLE: Osteoprotegerin in treatment of osteoporosis and other bone diseases

INVENTOR(S): Boyle, William J.; Lacey, David L.; Calzone, Frank J.; Chang, Ming-Shi

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: U.S., 117 pp., Cont. of U.S. Ser. No. 577,788.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 4

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6369027	B1	20020409	US 1996-706945	19960903
US 6613544	B1	20030902	US 1995-577788	19951222
DE 19654610	A1	19970626	DE 1996-19654610	19961220 <--
FR 2742767	A1	19970627	FR 1996-15707	19961220 <--
FR 2742767	B1	20010330		
CA 2210467	A1	19970703	CA 1996-2210467	19961220 <--
WO 9723614	A1	19970703	WO 1996-US20621	19961220 <--
W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN			
RW:	KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
EP 784093	A1	19970716	EP 1996-309363	19961220 <--
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AU 9714686	A	19970717	AU 1997-14686	19961220 <--
AU 710587	B2	19990923		
GB 2312899	A	19971112	GB 1996-26618	19961220 <--
GB 2312899	B	19990505		
CN 1182452	A	19980520	CN 1996-193441	19961220 <--
ZA 9610770	A	19980622	ZA 1996-10770	19961220 <--
HU 9801122	A2	19980828	HU 1998-1122	19961220 <--
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EP 870023	A1	19981014	EP 1996-945279	19961220 <--
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JP 11503616	T	19990330	JP 1996-523861	19961220
NZ 332915	A	20000728	NZ 1996-332915	19961220
CZ 292587	B6	20031015	CZ 1997-2538	19961220
PL 187408	B1	20040730	PL 1996-321938	19961220
EE 4643	B1	20060615	EE 1997-164	19961220
RO 121386	B1	20070430	RO 1997-1539	19961220
US 6284485	B1	20010904	US 1997-795445	19970206
US 6284728	B1	20010904	US 1997-795447	19970206
US 6288032	B1	20010911	US 1997-795446	19970206
TW 221482	B	20041001	TW 1997-86104638	19970411
BG 63347	B1	20011031	BG 1997-101813	19970805
NO 9703699	A	19971021	NO 1997-3699	19970812 <--
US 6015938	A	20000118	US 1997-974022	19971118
US 6284740	B1	20010904	US 1997-974186	19971118
US 20030207827	A1	20031106	US 1999-405032	19990924
AU 9965400	A	20000302	AU 1999-65400	19991222
AU 758672	B2	20030327		
US 7005413	B1	20060228	US 2000-613591	20000710
US 20050221331	A1	20051006	US 2004-762159	20040120
US 20050147611	A1	20050707	US 2005-58073	20050214
PRIORITY APPLN. INFO.:			US 1995-577788	A2 19951222
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			US 1996-771777	B1 19961220
			WO 1996-US20621	W 19961220
			US 1998-132985	A1 19980812
			US 1999-350670	B2 19990709
			US 1999-457647	B2 19991209
			US 2000-613591	A3 20000710

AB The present invention discloses a novel secreted polypeptide, osteoprotegerin, which is a member of the tumor necrosis factor receptor superfamily and is involved in the regulation of bone metabolism. Also disclosed are rat, mouse and human nucleic acids encoding

osteoprotegerin, polypeptides, recombinant vectors and host cells for expression, antibodies which bind OPG, and pharmaceutical compns. Expression of rat OPG cDNA in transgenic mouse showed increase in bone d., particularly in femurs, pelvic bones and vertebrae. C-terminal truncations of osteoprotegerin are provided that inhibit bone resorption. Specifically, amino acid residues 22-185 which comprise four cysteine-rich domains are required for osteoprotegerin activity. Furthermore, osteoprotegerin monomers may be linked by disulfide linkages and the dimeric form of OPG appears to predominate in transgenic mice, although trimeric forms may also exist. The polypeptides are used to treat bone diseases characterized by increased resorption such as osteoporosis.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 8 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoprotegerin

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(-binding protein; osteoprotegerin-binding protein receptors for therapeutic use)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 2001:829001 CAPLUS

DOCUMENT NUMBER: 135:367227

TITLE: Methods of use for osteoprotegerin-binding protein receptors

INVENTOR(S): Boyle, William J.

PATENT ASSIGNEE(S): Amgen Inc., USA

SOURCE: U.S., 59 pp., Cont.-in-part of U.S. Ser. No. 880,855.

CODEN: USXXAM

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
-----	----	-----	-----	-----
US 6316408	B1	20011113	US 1998-52521	19980330
US 5843678	A	19981201	US 1997-842842	19970416 <--
CA 2285746	A1	19981022	CA 1998-2285746	19980415 <--
WO 9846751	A1	19981022	WO 1998-US7584	19980415 <--
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9871205	A	19981111	AU 1998-71205	19980415 <--
AU 743257	B2	20020124		
EP 975754	A1	20000202	EP 1998-918244	19980415
EP 975754	B1	20070530		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, CY, AL, MK				
BR 9808545	A	20000523	BR 1998-8545	19980415
TR 9902512	T2	20000621	TR 1999-2512	19980415
HU 2000001400	A2	20000728	HU 2000-1400	19980415
HU 2000001400	A3	20011228		

EE 9900611	A	20000815	EE 1999-611	19980415
JP 2001526532	T	20011218	JP 1998-544257	19980415
NZ 500253	A	20020927	NZ 1998-500253	19980415
PL 190092	B1	20051031	PL 1998-336311	19980415
EP 1717315	A2	20061102	EP 2006-15956	19980415
EP 1717315	A3	20070620		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
AT 363533	T	20070615	AT 1998-918244	19980415
ES 2284203	T3	20071101	ES 1998-918244	19980415
ZA 9803189	A	19981016	ZA 1998-3189	19980416 <--
TW 589376	B	20040601	TW 1998-87105837	19980416
US 20030104485	A1	20030605	US 1998-79569	19980514
US 20030100488	A1	20030529	US 1998-211297	19981214
US 7097834	B1	20060829	US 1998-211315	19981214
MX 9909387	A	20000630	MX 1999-9387	19991013
NO 9905044	A	19991215	NO 1999-5044	19991015
NO 325175	B1	20080211		
BG 65242	B1	20070928	BG 1999-103824	19991021
HK 1022330	A1	20080215	HK 2000-101154	20000225
AU 2001095234	A	20020124	AU 2001-95234	20011130
AU 779461	B2	20050127		
US 20050003400	A1	20050106	US 2004-825898	20040415
AU 2005201799	A1	20050526	AU 2005-201799	20050427
AU 2005201799	B2	20080612		
US 20060246064	A1	20061102	US 2006-336067	20060119
JP 2008054682	A	20080313	JP 2007-228804	20070904

PRIORITY APPLN. INFO.:

US 1997-842842	A2	19970416
US 1997-880855	A2	19970623
US 1998-52521	A	19980330
AU 1998-71205	A3	19980415
EP 1998-918244	A3	19980415
JP 1998-544257	A3	19980415
WO 1998-US7584	W	19980415
US 1998-211315	A1	19981214
US 2000-721212	B1	20001121
AU 2001-95234	A3	20011130

AB A novel polypeptide, osteoprotegerin binding protein, involved in osteoclast maturation has been identified based upon its affinity for osteoprotegerin. Nucleic acid sequences encoding the polypeptide, or a fragment, analog or derivative thereof, vectors and host cells for production, methods of preparing osteoprotegerin binding protein, and binding assays are also described. Compns. and methods for the treatment of bone diseases such as osteoporosis, bone loss due to arthritis or metastasis, hypercalcemia, and Paget's disease are also provided. Receptors for osteoprotegerin binding proteins are also described. The receptors, and agonists and antagonists thereof, may be used to treat bone diseases.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 9 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoprotegerin

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(protein fragment complementation assays for detection of biol. or drug interactions)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 2001:703735 CAPLUS  
 DOCUMENT NUMBER: 135:269629  
 TITLE: Protein fragment complementation assays for the  
 detection of biological or drug interactions  
 INVENTOR(S): Michnick, Stephen William Watson; Remy, Ingrid  
 PATENT ASSIGNEE(S): Odyssey Pharmaceuticals Inc., USA  
 SOURCE: U.S., 41 pp., Cont.-in-part of U.S.6,290,964.  
 CODEN: USXXAM  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 13  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6294330	B1	20010925	US 1998-124850	19980730
CA 2196496	A1	19980731	CA 1997-2196496	19970131 <--
US 6270964	B1	20010807	US 1998-17412	19980202
EP 1605042	A2	20051214	EP 2005-17291	19980202
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CA 2244349	A1	20000130	CA 1998-2244349	19980730
WO 2000007038	A2	20000210	WO 1999-CA702	19990730
WO 2000007038	A3	20000504		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1027608	A2	20000816	EP 1999-936199	19990730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
US 20010047526	A1	20011129	US 2001-851084	20010509
US 6872871	B2	20050329		
US 20050233348	A1	20051020	US 2004-2259	20041203
US 20050255452	A1	20051117	US 2005-90215	20050328
AU 2005203580	A1	20050908	AU 2005-203580	20050811

PRIORITY APPLN. INFO.:  
 CA 1997-2196496 A 19970131  
 US 1998-17412 A2 19980202  
 EP 1998-901905 A3 19980202  
 CA 1998-2244349 A 19980730  
 US 1998-124850 A 19980730  
 WO 1999-CA702 W 19990730  
 US 2000-499464 A2 20000207  
 US 2000-203937P P 20000512  
 US 2000-208485P P 20000602  
 US 2001-851084 A3 20010509  
 US 2001-870018 A3 20010531  
 AU 2002-38204 A3 20020506

AB The invention provides a general protein-fragment complementation assays to detect biomol. interactions in vivo and in vitro. The protein-complementation assay/universal reporter system can be used to detect and screen an agonist and an antagonist of a membrane receptor system. The assay can be used to study protein-protein, protein-DNA, protein-RNA, protein-carbohydrate, and protein-small mol. interactions. The assay can be used to screen cDNA libraries for binding of a target protein with unknown proteins or libraries of small organic mols. for biol. activity. Dihydrofolate reductase fragments with leucine zipper motifs



were constructed for the reporter system.

L11 ANSWER 10 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 205944-50-9, Osteoclastogenesis inhibitory factor  
207621-35-0, Osteoclast differentiation factor  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
(Biological study); PROC (Process)  
(periodontal tissue remodeling incident to exptl. tooth movement in  
relation to mol. biol. and orthodontic treatment)  
RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 207621-35-0 CAPLUS  
CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1999:98526 CAPLUS  
DOCUMENT NUMBER: 130:306622  
TITLE: Periodontal tissue remodeling incident to experimental  
tooth movement  
AUTHOR(S): Kurihara, Saburo  
CORPORATE SOURCE: Department of Maxillofacial Oral Function, Institute  
for Dental Science, Matsumoto Dental University, Japan  
SOURCE: Matsumoto Shigaku (1998), 24(3), 237-251  
CODEN: MATSDE; ISSN: 0385-1613  
PUBLISHER: Matsumoto Shika Daigaku Gakkai  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: Japanese

AB A review, with 32 refs. Changes of periodontal tissues incident to exptl.  
tooth movement in vivo and mech. stress on bone tissue in vitro  
as well were explained and discussed in this article from the point of  
view of orthodontic treatment. These following items were introduced,  
based on results of basic and clin. researches. (1) Histol. structures of  
periodontal tissues and reaction of the tissues incident to exptl. tooth  
movement in vivo, (2) Tissue and cellular reaction related to mech.  
stimulus in vitro, (3) Recent topics of osteoclastogenesis inhibitory  
factor (OCIF) and osteoclast differentiation factor (ODF) related to mol.  
biol., (4) Prostaglandins as a mediator for bone resorption  
during orthodontic tooth movement, (5) Recent topics of orthodontic  
application for bone morphogenetic protein (BMP), (6)  
Application of results from the basic research of tooth movement on  
orthodontic treatment, such as optimum force, effective tooth movement and  
pharmacol. anchorage.

L11 ANSWER 11 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 207621-35-0P, Osteoclast differentiation factor  
RL: BAC (Biological activity or effector, except adverse); BPN  
(Biosynthetic preparation); BSU (Biological study, unclassified); BIOL  
(Biological study); PREP (Preparation)  
(osteoclastogenesis, control, and defects)  
RN 207621-35-0 CAPLUS  
CN Osteoclast differentiation factor (CA INDEX NAME)

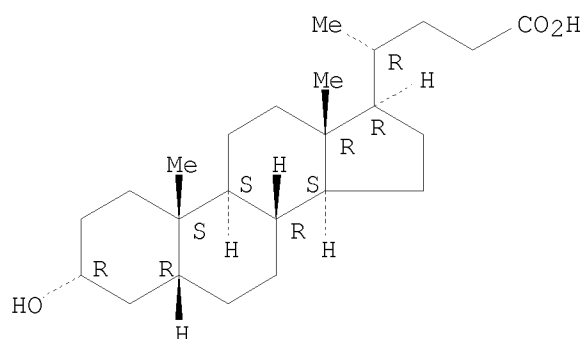
\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1999:51445 CAPLUS  
DOCUMENT NUMBER: 130:265150  
TITLE: Osteoclastogenesis, its control, and its defects  
AUTHOR(S): Abe, Etsuko; Yamate, Tomoo; Mocharla, Hanna; Taguchi,  
Yasuto; Yamamoto, Matsuo  
CORPORATE SOURCE: Department of Medicine, University of Arkansas for  
Medical Sciences, Little Rock, AR, USA

SOURCE: Advances in Organ Biology (1998),  
5B(Molecular and Cellular Biology of Bone), 289-313  
CODEN: AOBIFW  
PUBLISHER: JAI Press Inc.  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: English  
AB A review with .apprx.120 refs. In this chapter, the authors review recent findings regarding the origin and differentiation of osteoclasts and the role of hormones and cytokines in regulating this process, and the cloning of osteoclast differentiation factor (ODF). In addition, the authors introduce and discuss osteopetrotic bone disease caused by a defect in osteoclast development or function.  
REFERENCE COUNT: 141 THERE ARE 141 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 12 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 434-13-9  
RL: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); BIOL (Biological study); PROC (Process)  
(syntheses and preventive effects of analogs related to  
1 $\alpha$ ,25-dihydroxy-2 $\beta$ -(3-hydroxypropoxy)vitamin D3 (ED-71) on  
bone mineral loss in ovariectomized rats)  
RN 434-13-9 CAPLUS  
CN Cholan-24-oic acid, 3-hydroxy-, (3 $\alpha$ ,5 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 1999:38620 CAPLUS  
DOCUMENT NUMBER: 130:139508  
TITLE: Syntheses and preventive effects of analogs related to  
1 $\alpha$ ,25-dihydroxy-2 $\beta$ -(3-hydroxypropoxy)vitamin D3 (ED-71) on bone  
mineral loss in ovariectomized rats  
AUTHOR(S): Ono, Yoshiyuki; Kawase, Akira; Watanabe, Hiroyoshi;  
Shiraishi, Ayako; Takeda, Satoshi; Higuchi, Yoshinobu;  
Sato, Katsuhiko; Yamauchi, Tsuyoshi; Mikami,  
Tetsuhiro; Kato, Masahiro; Tsugawa, Naoko; Okano,  
Toshio; Kubodera, Noboru  
CORPORATE SOURCE: Chugai Pharmaceutical Co., Ltd., Tokyo, 104-8301,  
Japan  
SOURCE: Bioorganic & Medicinal Chemistry (1998),  
6(12), 2517-2523  
CODEN: BMECEP; ISSN: 0968-0896  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB    Analogs related to 1 $\alpha$ ,25-dihydroxy-2 $\beta$ -(3-hydroxypropoxy)vitamin D3 (ED-71), 26,27-dimethyl ED-71 and 26,27-diethyl ED-71, were synthesized from lithocholic acid. In the study of the preventive effects of these analogs and ED-71 on bone mineral loss in ovariectomized rats, 26,27-dimethyl ED-71 showed the most potent activity.

REFERENCE COUNT:            13        THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11   ANSWER 13 OF 46   CAPLUS   COPYRIGHT 2008 ACS on STN

IT    205944-50-9, Osteoclastogenesis inhibitory factor  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
      (osteoclastogenesis inhibitory factor exhibits hypocalcemic effects in normal mice and in hypercalcemic nude mice carrying tumors associated with humoral hypercalcemia of malignancy)

RN    205944-50-9   CAPLUS

CN    Osteoprotegerin   (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER:            1999:5743   CAPLUS

DOCUMENT NUMBER:            130:218668

TITLE:                        Osteoclastogenesis inhibitory factor exhibits hypocalcemic effects in normal mice and in hypercalcemic nude mice carrying tumors associated with humoral hypercalcemia of malignancy

AUTHOR(S):                   Akatsu, T.; Murakami, T.; Ono, K.; Nishikawa, M.; Tsuda, E.; Mochizuki, S.-I.; Fujise, N.; Higashio, K.; Motoyoshi, K.; Yamamoto, M.; Nagata, N.

CORPORATE SOURCE:            Third Department of Internal Medicine, National Defense Medical College, Saitama, 359, Japan

SOURCE:                      Bone (New York) (1998), 23(6), 495-498

CODEN: BONEDL; ISSN: 8756-3282

PUBLISHER:                   Elsevier Science Inc.

DOCUMENT TYPE:               Journal

LANGUAGE:                    English

AB    Osteoclastogenesis inhibitory factor (OCIF) is a novel secreted protein that inhibits osteoclastogenesis both in vitro and in vivo. In this study, we examined the effects of OCIF on serum calcium (Ca) concns. in normal mice and in hypercalcemic nude mice carrying tumors associated with humoral hypercalcemia of malignancy. In normal mice, a single i.p. injection of OCIF reduced serum Ca levels in a dose-dependent manner. Significant decrease in serum Ca (by 1.6 mg/dL) was observed 2 h after the injection of OCIF at 20 mg/kg and the hypocalcemic effect continued for up to 12 h. Serum phosphate (Pi) concns. also decreased in response to OCIF. Urinary excretion of Ca, Pi, and creatinine did not change significantly after injection of OCIF or vehicle. In hypercalcemic, tumor-bearing nude mice, a single i.p. injection of OCIF at 20 mg/kg resulted in a dramatic decrease in serum Ca (maximal decrease 2.8 mg/dL), which continued for up to 24 h. The results suggest that OCIF decreased serum Ca through its inhibitory effect on bone resorption. Furthermore, it is suggested that OCIF has therapeutic potential for the treatment of hypercalcemic conditions such as malignancy-associated hypercalcemia.

REFERENCE COUNT:            16        THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11   ANSWER 14 OF 46   CAPLUS   COPYRIGHT 2008 ACS on STN

IT    205944-50-9, Osteoclastogenesis inhibitory factor  
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)  
      (TGF- $\beta$ 1 increases osteoclastogenesis inhibitory factor expression

in osteoblastic/stromal cells and inhibits murine osteoclast like-cell survival)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:799358 CAPLUS

DOCUMENT NUMBER: 130:119996

TITLE: Transforming growth factor- $\beta$ 1 increases mRNA levels of osteoclastogenesis inhibitory factor in osteoblastic/stromal cells and inhibits the survival of murine osteoclast-like cells

AUTHOR(S): Murakami, Takehiko; Yamamoto, Michiko; Yamamoto, Mikio; Ono, Katsuhiko; Nishikawa, Miyuki; Nagata, Naokazu; Motoyoshi, Kazuo; Akatsu, Takuhiko

CORPORATE SOURCE: Third Department of Internal Medicine, National Defense Medical College, Saitama, 359-8513, Japan

SOURCE: Biochemical and Biophysical Research Communications (1998), 252(3), 747-752

CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Osteoclastogenesis inhibitory factor (OCIF) is a secreted member of the tumor necrosis factor (TNF) receptor family. It inhibits bone resorption in vivo and osteoclast-like cell (OCL) formation in vitro. To better understand the biol. role of OCIF, we first examined the effects of various osteotropic agents on OCIF mRNA levels in mouse calvarial osteoblasts. Northern blot anal. showed that stimulators of OCL formation such as 1,25-(OH) $_2$ D $_3$ , prostaglandin E $_2$  (PGE $_2$ ), parathyroid hormone (PTH), and interleukin 1 (IL-1) decreased OCIF mRNA levels. In contrast, transforming growth factor (TGF)- $\beta$ 1 increased OCIF mRNA levels in primary osteoblasts as well as in osteoblastic/stromal cell lines. Since it was reported that both TGF- $\beta$ 1 and OCIF not only inhibited OCL formation but also impaired the survival of OCL by inducing apoptosis in vitro, we next examined the possible involvement of OCIF in TGF- $\beta$ 1-induced impairment of OCL survival. In a mouse bone marrow culture, we confirmed that addition of OCIF or TGF- $\beta$ 1 decreased the number of surviving OCL. Anti-OCIF IgG, which completely neutralized the effect of OCIF, partially prevented the TGF- $\beta$ 1-induced decrease in the number of OCL. Our results suggest that (i) downregulation of OCIF expression is one of the mechanisms for the stimulatory effects of 1,25(OH) $_2$ D $_3$ , PGE $_2$ , PTH, and IL-1 on osteoclastogenesis; and (ii) the TGF- $\beta$ 1-induced apoptosis of OCL is mediated, at least in part, by upregulation of OCIF expression. (c) 1998 Academic Press.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 15 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 207621-35-0, Osteoclast differentiation factor

RL: BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)

(transcription factor Cbfa1 regulation of mRNA expression of osteoclast differentiation factor in osteoclastogenesis)

RN 207621-35-0 CAPLUS

CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:799349 CAPLUS

DOCUMENT NUMBER: 130:137277

TITLE: Potential role of Cbfa1, an essential transcriptional factor for osteoblast differentiation, in

osteoclastogenesis: regulation of mRNA expression of  
osteoclast differentiation factor (ODF)  
AUTHOR(S): Gao, Yu-Hao; Shinki, Toshimasa; Yuasa, Takahito;  
Kataoka-Enomoto, Hiroko; Komori, Toshihisa; Suda,  
Tatsuo; Yamaguchi, Akira  
CORPORATE SOURCE: Department of Oral Pathology, School of Dentistry,  
Showa University, Tokyo, 142-8555, Japan  
SOURCE: Biochemical and Biophysical Research Communications ( 1998), 252(3), 697-702  
CODEN: BBRCA9; ISSN: 0006-291X  
PUBLISHER: Academic Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The role of Cbfa1 (core binding factor  $\alpha$ 1), an essential transcriptional factor for osteoblast differentiation, in osteoclastogenesis was investigated in vitro and in vivo using Cbfa1-deficient calvarial cells and mice. Co-cultures of calvarial cells isolated from embryos with three different Cbfa1 genotypes (Cbfa1+/+, Cbfa1+/- and Cbfa1-/-) and normal spleen cells generated TRAP-pos. multinucleated osteoclast-like cells (OCLs) in response to  $1\alpha,25$ -dihydroxyvitamin D3 [ $1\alpha,25$ (OH)2D3] and dexamethasone, but the number and bone-resorbing activity of OCLs formed in co-culture with Cbfa1-/- calvarial cells were significantly decreased in comparison with those formed in co-cultures with Cbfa1+/+ or Cbfa1+/- calvarial cells. The expression of osteoclast differentiation factor/osteoprotegerin ligand (ODF/OPGL) mRNA was increased by the treatment with  $1\alpha,25$ (OH)2D3 and dexamethasone in calvarial cells from Cbfa1+/+ and Cbfa1+/- mouse embryos, but not from Cbfa1-/- embryos. In contrast, the expression of osteoprotegerin/osteoclastogenesis inhibitory factor (OPG/OCIF) mRNA was inhibited by  $1\alpha,25$ (OH)2D3 and dexamethasone similarly in all three types of calvarial cells. ODF/OPGL and OPG/OCIF mRNAs were highly expressed in the tibia and femur of Cbfa1+/+ and Cbfa1+/- embryos. In the tibia and femur of Cbfa1-/- embryos, however, ODF/OPGL mRNA was undetectable and the expression of OPG/OCIF mRNA was also decreased compared with those in Cbfa1+/+ and Cbfa1+/- embryos. These results suggested that Cbfa1 is somehow involved in osteoclastogenesis through regulation of ODF/OPGL. (c) 1998 Academic Press.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 16 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoclastogenesis inhibitory factor  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(osteoclastogenesis inhibitory factor regulation of bone resorption)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:769598 CAPLUS

DOCUMENT NUMBER: 130:148742

TITLE: Osteoclastogenesis inhibitory factor (OCIF/OPG) and control of bone resorption

AUTHOR(S): Anon.

CORPORATE SOURCE: Japan

SOURCE: Rinsho Kagaku (Osaka) (1998), 34(10), 1387-1392

CODEN: RIKAE9; ISSN: 0385-0323

PUBLISHER: Esuato K. K.

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review with 26 refs., on research in OCIF, discussing osteoclast differentiation factor as target mol. for OCIF; OCIF in bone resorption; and OCIF genes.

L11 ANSWER 17 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoclastogenesis inhibitory factor

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(osteoclastogenesis inhibitory factor directly inhibits bone  
-resorbing activity of isolated mature osteoclasts)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:732139 CAPLUS

DOCUMENT NUMBER: 130:61553

TITLE: Osteoclastogenesis inhibitory factor (OCIF) directly  
inhibits bone-resorbing activity of isolated  
mature osteoclasts

AUTHOR(S): Hakeda, Yoshiyuki; Kobayashi, Yukinao; Yamaguchi,  
Kyoji; Yasuda, Hisataka; Tsuda, Eisuke; Higashio,  
Koji; Miyata, Takashi; Kumegawa, Masayoshi

CORPORATE SOURCE: Department of Oral Anatomy, School of Dentistry,  
Meikai University, Sakado, Saitama, 350-0283, Japan

SOURCE: Biochemical and Biophysical Research Communications (1998), 251(3), 796-801

CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Osteoclastogenesis inhibitory factor (OCIF) was previously reported to specifically inhibit osteoclast development by interrupting the action of osteoclast differentiation factor (ODF), which is expressed in stromal cells and plays an important role in osteoclastogenesis. Here we report the direct action of OCIF on isolated rabbit mature osteoclasts to inhibit their functional bone-resorbing activity. The cell population employed in this study consisted of mature osteoclasts with more than 95% of purity. The inhibition by OCIF was dose dependent and observed as early as 6 h after the OCIF addition. An OCIF-binding protein of 140 kDa was detected on the plasma membrane of osteoclasts. ODF with a Mr of 40 kDa was recently isolated as a ligand for OCIF and shows to be identical to TRANCE/RANKL. However, ODF was not detected in osteoclasts. OCIF did not have any impact on the mRNA levels of cathepsin K/OC2 and carbonic anhydrase II responsible for degradation of organic and inorg. bone matrixes, resp., or on osteoclast apoptosis. However, OCIF reduced or disrupted the formation of F-actin ring in isolated osteoclasts, the cytoskeletal structure of which is correlated with bone resorption. These findings demonstrate that OCIF directly inhibits osteoclast function through an ODF-independent mechanism besides blocking the generation of osteoclasts. (c) 1998 Academic Press.

REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 18 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 207621-35-0, Osteoclast differentiation factor

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(TGF- $\beta$  stimulates osteoclastogenesis inhibitory factor formation  
by bone marrow stromal cells)

RN 207621-35-0 CAPLUS

CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 205944-50-9, Osteoclastogenesis inhibitory factor  
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM  
(Metabolic formation); BIOL (Biological study); FORM (Formation,  
nonpreparative); PROC (Process)  
(TGF- $\beta$  stimulates osteoclastogenesis inhibitory factor formation  
by bone marrow stromal cells)  
RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:700244 CAPLUS  
DOCUMENT NUMBER: 130:33474  
TITLE: Transforming growth factor- $\beta$  stimulates the  
production of osteoprotegerin/osteoclastogenesis  
inhibitory factor by bone marrow stromal  
cells  
AUTHOR(S): Takai, Hiroyuki; Kanematsu, Masahiro; Yano, Kazuki;  
Tsuda, Eisuke; Higashio, Kanji; Ikeda, Kyoji;  
Watanabe, Ken; Yamada, Yoshiji  
CORPORATE SOURCE: Department of Geriatric Research, National Institute  
for Longevity Sciences, Aichi, 474-8522, Japan  
SOURCE: Journal of Biological Chemistry (1998),  
273(42), 27091-27096  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular  
Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Osteoprotegerin (OPG)/osteoclastogenesis inhibitory factor (OCIF) is a recently identified cytokine that belongs to the tumor necrosis factor receptor superfamily and regulates bone mass by inhibiting osteoclastic bone resorption. The present study was undertaken to determine whether OPG/OCIF is produced in bone microenvironment and how the expression is regulated. A transcript for OPG/OCIF at 3.1 kilobases was detected in bone marrow stromal cells (ST2 and MC3T3-G2/PA6) as well as in osteoblastic cells (MC3T3-E1). Transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1) markedly increased the steady-state level of OPG/OCIF mRNA in a dose-dependent manner, while TGF- $\beta$ 1 suppressed the mRNA expression of tumor necrosis factor-related activation-induced cytokine (TRANCE)/receptor activator of NF- $\kappa$ B ligand (RANKL), a pos. regulator of osteoclastogenesis to which OPG/OCIF binds. The effect of TGF- $\beta$ 1 on the expression of OPG/OCIF mRNA was transient, with a peak level at 3-6 h. The up-regulation of OPG/OCIF mRNA by TGF- $\beta$ 1 in ST2 cells did not require de novo protein synthesis and involved both a transcriptional and a post-transcriptional mechanism. Western blot anal. and an ELISA revealed that TGF- $\beta$ 1 significantly increased the secretion of OPG/OCIF protein by ST2 cells at 6-24 h. In murine bone marrow cultures, TGF- $\beta$ 1 markedly inhibited the formation of tartrate-resistant acid phosphatase-pos. multinucleated osteoclast-like cells in the presence of 1,25-dihydroxyvitamin D3, whose effect was significantly reversed by a neutralizing antibody against OPG/OCIF. These results suggest that TGF- $\beta$ 1 neg. regulates osteoclastogenesis, at least in part, through the induction of OPG/OCIF by bone marrow stromal cells and that the balance between OPG/OCIF and TRANCE/RANKL in local environment may be an important determinant of osteoclastic bone resorption.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

IT 205944-50-9, Osteoclastogenesis inhibitory factor  
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)  
(osteoprotegerin production by human osteoblast lineage cells stimulation by vitamin D and bone morphogenetic protein-2 and cytokines)  
RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:659940 CAPLUS  
DOCUMENT NUMBER: 130:829  
TITLE: Osteoprotegerin production by human osteoblast lineage cells is stimulated by vitamin D, bone morphogenetic protein-2, and cytokines  
AUTHOR(S): Hofbauer, Lorenz C.; Dunstan, Colin R.; Spelsberg, Thomas C.; Riggs, B. Lawrence; Khosla, Sundeep  
CORPORATE SOURCE: Endocrine Research Unit, Mayo Clinic and Mayo Foundation, Rochester, MN, USA  
SOURCE: Biochemical and Biophysical Research Communications ( 1998), 250(3), 776-781  
CODEN: BBRCA9; ISSN: 0006-291X  
PUBLISHER: Academic Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Osteoprotegerin (OPG), a newly discovered member of the tumor necrosis factor receptor family, is a potent inhibitor of osteoclastogenesis. The overexpression of OPG in transgenic mice leads to osteopetrosis, whereas targeted ablation of OPG in knock-out mice leads to severe osteoporosis. However, the production and regulation of OPG in normal human bone has not been studied. Thus, we assessed OPG mRNA expression and protein secretion in human osteoblastic lineage cells. 1,25-Dihydroxyvitamin D3 ( $10^{-7}$  M) increased OPG mRNA levels by 90 and 50% in a fetal osteoblastic cell line (hFOB) and normal trabecular osteoblastic cells (hOB) cells, resp., but did not affect OPG mRNA levels in a marrow stromal preosteoblastic (hMS) cell line. Interleukin (IL)- $1\beta$  ( $5 + 10^{-9}$  M), tumor necrosis factor (TNF)- $\alpha$  ( $9 + 10^{-9}$  M), and bone morphogenetic protein (BMP)-2 (100 ng/mL) also increased OPG mRNA levels in hFOB cells by 4-, 6-, and 4-fold, resp. Treatment with 1,25-dihydroxyvitamin D3, IL- $1\beta$ , TNF- $\alpha$ , and BMP-2 increased OPG protein production by hFOB cells by 60, 390, 300, and 80%, resp. Because it is expressed in various types of human osteoblastic cells, and is stimulated by vitamin D, BMP-2 and cytokines, OPG may be an important paracrine modulator of bone remodeling. (c) 1998 Academic Press.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 20 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoclastogenesis inhibitory factor  
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); OCCU (Occurrence); PROC (Process)  
(osteoprotegerin mRNA expression in primary human osteoblast-like cells down-regulation by glucocorticoids)  
RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:657485 CAPLUS  
DOCUMENT NUMBER: 130:629  
TITLE: Osteoprotegerin mRNA is expressed in primary human



osteoblast-like cells: down-regulation by glucocorticoids

AUTHOR(S): Vidal, N. O. A.; Brandstrom, H.; Jonsson, K. B.; Ohlsson, C.

CORPORATE SOURCE: Research Centre for Endocrinology and Metabolism, Department of Internal Medicine, Sahlgrenska University Hospital, Goeteborg, Swed.

SOURCE: Journal of Endocrinology (1998), 159(1), 191-195

CODEN: JOENAK; ISSN: 0022-0795

PUBLISHER: Society for Endocrinology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Osteoprotegerin (OPG) is a recently cloned member of the tumor necrosis factor receptor family. It has been suggested that this secreted glycoprotein acts as an inhibitor of osteoclastic differentiation. Expression of OPG has previously been demonstrated in a number of tissues. However, it is still unclear whether or not OPG is expressed by human osteoblasts. The authors have used the RNase protection assay to demonstrate the OPG transcript in primary cultured human osteoblast-like cells, human marrow stroma cells and osteosarcoma cell lines. Furthermore, the authors have studied the effect of glucocorticoids on OPG mRNA levels in these cells. The authors demonstrate that glucocorticoids decrease the OPG transcript in a dose- and time-dependent manner. The time-course study reveals that hydrocortisone ( $10^{-6}$  M) decreases OPG mRNA levels within 2 h. This decrease is transient, reaching control levels again after 24 h. The findings demonstrate that human osteoblasts express the mRNA corresponding to OPG, an inhibitor of osteoclast differentiation. The finding that OPG mRNA levels are decreased by glucocorticoids indicates that a reduced production of OPG from osteoblasts and/or marrow stroma cells could, in part, explain glucocorticoid-induced bone resorption.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 21 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 207621-35-0, Osteoclast differentiation factor

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(osteoclast differentiation factor and macrophage-colony stimulating factor combination stimulate human and mouse osteoclast formation in vitro)

RN 207621-35-0 CAPLUS

CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:645523 CAPLUS

DOCUMENT NUMBER: 129:326551

ORIGINAL REFERENCE NO.: 129:66471a,66474a

TITLE: A combination of osteoclast differentiation factor and macrophage-colony stimulating factor is sufficient for both human and mouse osteoclast formation in vitro

AUTHOR(S): Quinn, Julian M. W.; Elliott, Jan; Gillespie, Matthew T.; Martin, T. John

CORPORATE SOURCE: Department of Medicine and St Vincent's Institute of Medical Research, The University of Melbourne, Fitzroy, 3065, Australia

SOURCE: Endocrinology (1998), 139(10), 4424-4427

CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Both human and murine osteoclasts can be derived in vitro from hematopoietic cells or monocytes that are cocultured with osteoblasts or marrow-derived stromal cells. The osteoclastogenic stimulus provided by murine osteoblasts and marrow-derived stromal cells is now known to be mediated by osteoclast differentiation factor (ODF), a membrane-bound tumor necrosis factor-related ligand. This study demonstrates that mouse spleen cells and monocytes form osteoclasts when cultured in the presence of macrophage-colony stimulating factor (M-CSF) and a soluble form of murine ODF (sODF). Numerous multinucleated osteoclasts expressing tartrate-resistant acid phosphatase (TRAP) and calcitonin receptor (CTR) formed within 7 days of culture and engaged in extensive lacunar bone resorption. Osteoclast number and bone resorption area was dependent on sODF concentration Long-term cultured human monocytes

also

formed bone resorbing osteoclasts in response to co-stimulation by sODF and M-CSF, although this required more than 11 days in culture. This human osteoclast differentiation was strongly inhibited by granulocyte-macrophage colony stimulating factor. This study further characterizes murine osteoclast differentiation caused by sODF and M-CSF co-stimulation in vitro, and shows that the same co-stimulation causes human osteoclast differentiation to occur. The authors propose that this methodol. can be employed to investigate the direct effects of cytokines and other factors on human osteoclast differentiation.

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 22 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoclastogenesis inhibitory factor

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(osteoclastogenesis inhibitory factor suppresses osteoclast survival by interfering in interaction of stromal cells with osteoclast)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:628318 CAPLUS

DOCUMENT NUMBER: 130:796

TITLE: Osteoclastogenesis inhibitory factor suppresses osteoclast survival by interfering in the interaction of stromal cells with osteoclast

AUTHOR(S): Akatsu, Takuhiko; Murakami, Takehiko; Nishikawa, Miyuki; Ono, Katsuhiko; Shinomiya, Nariyoshi; Tsuda, Eisuke; Mochizuki, Shin-Ichi; Yamaguchi, Kyoji; Kinoshita, Masahiko; Higashio, Kanji; Yamamoto, Michiko; Motoyoshi, Kazuo; Nagata, Naokazu

CORPORATE SOURCE: Third Department of Internal Medicine, National Defense Medical College, Tokorozawa, Saitama, 359-8513, Japan

SOURCE: Biochemical and Biophysical Research Communications ( 1998), 250(2), 229-234  
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Osteoclastogenesis inhibitory factor (OCIF) was originally identified as a factor inhibiting osteoclast (OC) formation. The number of OC in rats treated with OCIF decreased, suggesting that OCIF inhibits OC formation in vivo; however, it is also possible that OCIF affects the number of OC by promoting apoptosis of OC. To address this issue, the effects of OCIF on the survival of OC were examined using well established mouse culture systems. OCIF dose-dependently inhibited OC formation in mouse marrow

cultures. Addition of OCIF during day 0-3 did not alter the peak levels of OC formation on day 7 and 8. However, the addition of OCIF during day 5 and thereafter resulted in the rapid decrease of the number of OC. OCIF inhibited the survival of OC formed in mouse marrow cultures in dose- and time-dependent manners. The involvement of stromal cells in OC survival was examined using crude and stromal cell-depleted OC populations. OCIF dramatically inhibited the survival of crude OC populations rich with stromal cells. However, in stromal cell-depleted OC populations, OC spontaneously decreased in the absence of OCIF and OCIF did not enhance the decrease further at least up to 48 h. Apoptotic OC were detected in detached cell populations treated with OCIF in mouse marrow cultures and a specific inhibitor for caspase-3 rescued the death of OC. OCIF mutant lacking the death domain homologous regions inhibited OC survival, though the potency was much less than native OCIF. Taken together, OCIF inhibited not only OC recruitment but also OC survival. OCIF inhibited OC survival by interfering the interaction of stromal cells with OC. (c) 1998 Academic Press.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 23 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 205944-50-9, Osteoclastogenesis inhibitory factor  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(osteoclastogenesis inhibitory factor/osteoprotegerin regulation of bone resorption)  
RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
IT 207621-35-0, Osteoclast differentiation factor  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(osteoclastogenesis inhibitory factor/osteoprotegerin regulation of bone resorption)  
RN 207621-35-0 CAPLUS  
CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
ACCESSION NUMBER: 1998:621418 CAPLUS  
DOCUMENT NUMBER: 130:10737  
TITLE: Regulation of bone resorption by a novel cytokine termed OCIF/osteoprotegerin  
AUTHOR(S): Morinaga, Tomonori; Higashio, Kanji  
CORPORATE SOURCE: Inst. Life Sci., Snow Brand Milk Prod. Co., Ltd., Tochigi, 329-0512, Japan  
SOURCE: Bone (Osaka) (1998), 12(3), 77-84  
CODEN: BONEFN; ISSN: 0914-7047  
PUBLISHER: Medikaru Rebyusha  
DOCUMENT TYPE: Journal; General Review  
LANGUAGE: Japanese  
AB A review with 24 refs. Osteoclastogenesis inhibitory factor (OCIF) suppresses differentiation and maturation of osteoclast cells secreted by human fetal lung fibroblast cells, IMR-90, and is identical to osteoprotegerin (OPG) derived from a severe osteopetrosis mouse. OCIF/OPG possesses death domain homolog (DDH), which possesses capability to induce apoptosis. OCIF/OPG is expressed in most tissues except peripheral blood lymphocytes, and its expression is regulated by Ca concentration OCIF/OPG suppresses osteoclast generation by binding with osteoclast differentiation factor (ODF). The action mechanisms of OCIF/OPG and ODF are depicted.

L11 ANSWER 24 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 205944-50-9, Osteoclastogenesis inhibitory factor  
207621-35-0, Osteoclast differentiation factor  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(TRANCE necessary and sufficient for osteoblast-mediated activation of bone resorption in osteoclasts)  
RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 207621-35-0 CAPLUS  
CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:602371 CAPLUS  
DOCUMENT NUMBER: 129:314804  
ORIGINAL REFERENCE NO.: 129:64233a,64236a  
TITLE: TRANCE is necessary and sufficient for osteoblast-mediated activation of bone resorption in osteoclasts  
AUTHOR(S): Fuller, Karen; Wong, Brian; Fox, Simon; Choi, Yongwon; Chambers, Tim J.  
CORPORATE SOURCE: St. George's Hospital Medical School, London, SW17 ORE, UK  
SOURCE: Journal of Experimental Medicine (1998), 188(5), 997-1001  
CODEN: JEMEAV; ISSN: 0022-1007  
PUBLISHER: Rockefeller University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB TRANCE (tumor necrosis factor-related activation-induced cytokine) is a recently described member of the tumor necrosis factor superfamily that stimulates dendritic cell survival and has also been found to induce osteoclastic differentiation from hemopoietic precursors. However, its effects on mature osteoclasts have not been defined. It has long been recognized that stimulation of osteoclasts by agents such as parathyroid hormone (PTH) occurs through a hormonal interaction with osteoblastic cells, which are thereby induced to activate osteoclasts. To determine whether TRANCE accounts for this activity, we tested its effects on mature osteoclasts. TRANCE rapidly induced a dramatic change in osteoclast motility and spreading and inhibited apoptosis. In populations of osteoclasts that were unresponsive to PTH, TRANCE caused activation of bone resorption equivalent to that induced by PTH in the presence of osteoblastic cells. Moreover, osteoblast-mediated stimulation of bone resorption was abrogated by soluble TRANCE receptor and by the soluble decoy receptor osteoprotegerin (OPG), and stimulation of isolated osteoclasts by TRANCE was neutralized by OPG. Thus, TRANCE expression by osteoblasts appears to be both necessary and sufficient for hormone-mediated activation of mature osteoclasts, and TRANCE-R is likely to be a receptor for signal transduction for activation of the osteoclast and its survival.

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 25 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 205944-50-9, Osteoclastogenesis inhibitory factor  
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(structure of mouse osteoclastogenesis inhibitory factor (OCIF) gene and its expression in embryogenesis)

RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:590273 CAPLUS  
DOCUMENT NUMBER: 129:286629  
ORIGINAL REFERENCE NO.: 129:58309a,58312a  
TITLE: Structure of the mouse osteoclastogenesis inhibitory factor (OCIF) gene and its expression in embryogenesis  
AUTHOR(S): Mizuno, Atsuko; Murakami, Akihiko; Nakagawa, Nobuaki; Yasuda, Hisataka; Tsuda, Eisuke; Morinaga, Tomonori; Higashio, Kanji  
CORPORATE SOURCE: Research Institute of Life Science, Snow Brand Milk Products, Co. Ltd, Ishibashi-machi, Shimotsuga-gun, Tochigi, 329-0512, Japan  
SOURCE: Gene (1998), 215(2), 339-343  
CODEN: GENED6; ISSN: 0378-1119  
PUBLISHER: Elsevier Science B.V.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Osteoclastogenesis inhibitory factor (OCIF) is a novel soluble-form member of the tumor necrosis factor receptor family and is involved in the regulation of bone mass. Here the authors isolated genomic and cDNA clones for mouse OCIF and determined their structures. Mouse OCIF gene spans 29 kb and contains five exons of 270, 367, 192, 225 and 1765 bp long. Four cysteine-rich domains and two death domain homologous regions characterized in human OCIF are rigidly conserved in mouse OCIF. The onset of OCIF gene expression in mouse embryogenesis is at day 8.5. In a pregnant female mouse, OCIF gene is expressed in decidua, a maternal tissue surrounding each embryo, immediately after implantation. The isolation of mouse OCIF gene should facilitate studies on OCIF knock-out mice for a better understanding of the role of OCIF in vivo.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 26 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoclastogenesis inhibitory factor  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(hypocalcemic effect of osteoclastogenesis inhibitory factor/osteoprotegerin in thyroparathyroidectomized rat)

RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:557213 CAPLUS  
DOCUMENT NUMBER: 129:255507  
ORIGINAL REFERENCE NO.: 129:51923a,51926a  
TITLE: Hypocalcemic effect of osteoclastogenesis inhibitory factor/osteoprotegerin in the thyroparathyroidectomized rat  
AUTHOR(S): Yamamoto, Michiko; Murakami, Takehiko; Nishikawa, Miyuki; Tsuda, Eisuke; Mochizuki, Shin-Ichi; Higashio, Kanji; Akatsu, Takuhiko; Motoyoshi, Kazuo; Nagata, Naokazu  
CORPORATE SOURCE: Third Department of Internal Medicine, National Defense Medical College, Saitama, 359-8513, Japan  
SOURCE: Endocrinology (1998), 139(9), 4012-4015  
CODEN: ENDOAO; ISSN: 0013-7227  
PUBLISHER: Endocrine Society  
DOCUMENT TYPE: Journal

LANGUAGE: English

AB Osteoclastogenesis inhibitory factor (OCIF), also termed as osteoprotegerin (OPG), is a soluble member of the tumor necrosis factor receptor family. Although OCIF/OPG is shown to inhibit osteoclast formation in vitro and prevent ovariectomy-induced bone loss in vivo, its effect on serum calcium level remains to be determined. In this study the authors examined the acute effect of OCIF on thyroparathyroidectomized rats whose serum calcium concns. were raised either by exogenous PTH or 1,25-(OH)2D3. When OCIF was administered at the start of PTH infusion, it attenuated the initial rise in serum calcium. When OCIF was administered into rats with established hypercalcemia, it decreased serum calcium rapidly (within 2 h) and dramatically. OCIF did not increase urinary calcium excretion. These findings, especially the rapid onset of its hypocalcemic effect, suggest that OCIF not only inhibits the formation of osteoclasts but also affects the function and/or survival of mature osteoclasts at doses used in this study.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 27 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoclastogenesis inhibitory factor  
207621-35-0, Osteoclast differentiation factor  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)  
(osteoprotegerin and its cognate ligand: a new paradigm of osteoclastogenesis)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

RN 207621-35-0 CAPLUS

CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:549094 CAPLUS

DOCUMENT NUMBER: 129:274334

ORIGINAL REFERENCE NO.: 129:55929a

TITLE: Osteoprotegerin and its cognate ligand: a new paradigm of osteoclastogenesis

AUTHOR(S): Hofbauer, Lorenz C.; Heufelder, Armin E.

CORPORATE SOURCE: Endocrine Research Unit, Mayo Clinic, Rochester, MN, 55905, USA

SOURCE: European Journal of Endocrinology (1998), 139(2), 152-154

CODEN: EJOEEP; ISSN: 0804-4643

PUBLISHER: BioScientifica

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review and discussion with 11 refs. Osteoprotegerin (OPG) is a member of the tumor necrosis factor receptor superfamily. OPG and its cognate ligand (OPGL) are a cybernetic couple that regulate bone mass by modulating osteoclastogenesis. OPGL seems to be the endogenous master cytokine, which is the condition sine qua non for normal osteoclast differentiation and activation, whereas OPG is a naturally occurring soluble receptor that counterbalances the effects of OPGL and preserves bone mass. Mechanisms of action of OPG and OPGL are presented.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 28 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoclastogenesis inhibitory factor

RL: BOC (Biological occurrence); BSU (Biological study, unclassified);  
BIOL (Biological study); OCCU (Occurrence)  
(osteoprotegerin (OPG); osteoprotegerin mRNA is increased by  
interleukin-1 $\alpha$  in human osteosarcoma cell line MG-63 and in human  
osteoblast-like cells)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:522865 CAPLUS

DOCUMENT NUMBER: 129:243899

ORIGINAL REFERENCE NO.: 129:49646h, 49647a

TITLE: Osteoprotegerin mRNA is increased by  
interleukin-1 $\alpha$  in the human osteosarcoma cell  
line MG-63 and in human osteoblast-like cells

AUTHOR(S): Vidal, Olle N. A.; Sjogren, Klara; Eriksson, Bengt I.;  
Ljunggren, Osten; Ohlsson, Claes

CORPORATE SOURCE: Endocrine Bone Unit, Research Center for Endocrinology  
and Metabolism, Goeteborg, Swed.

SOURCE: Biochemical and Biophysical Research Communications ( 1998), 248(3), 696-700

CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Osteoprotegerin (OPG) is a soluble receptor for the osteoprotegerin-ligand (OPGL) which is expressed on osteoblasts and mediates the signal for osteoclast differentiation. Here, the authors demonstrate that OPG mRNA levels in MG-63 cells are increased in a dose-dependent manner after 8 h of treatment with IL-1 $\alpha$  (338% over control at 25 U/mL). Interleukin-6 (IL-6), under similar culture conditions, does not affect OPG mRNA levels. Time-course studies show that IL-1 $\alpha$  (25 U/mL) causes a transient increase of OPG mRNA levels in MG-63 cells, peaking after 4 h of treatment. An increase of the OPG transcript occurs in hOB cells at 0.5 h which is still present after 24 h of IL-1 $\alpha$  treatment. In MG-63 cells neither basal- nor IL-1 $\alpha$ -induced OPG mRNA levels are altered by the translational inhibitor cycloheximide. Thus, expression of OPG in osteoblasts may be regulated by IL-1 $\alpha$ . (c) 1998 Academic Press.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 29 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoclastogenesis inhibitory factor

RL: BOC (Biological occurrence); BSU (Biological study, unclassified);  
BIOL (Biological study); OCCU (Occurrence)

(OPG (osteoprotegerin); tumor necrosis factor- $\alpha$  and - $\beta$   
upregulation of osteoprotegerin mRNA in human osteoblasts in relation  
to bone resorption)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:522821 CAPLUS

DOCUMENT NUMBER: 129:229516

ORIGINAL REFERENCE NO.: 129:46697a, 46700a

TITLE: Tumor necrosis factor- $\alpha$  and - $\beta$  upregulate  
the levels of osteoprotegerin mRNA in human  
osteosarcoma MG-63 cells

AUTHOR(S): Brandstrom, Helena; Jonsson, Kenneth B.; Vidal, Olle;  
Ljunghall, Sverker; Ohlsson, Claes; Ljunggren, Osten

CORPORATE SOURCE: Department of Medical Sciences, University of Uppsala,

Uppsala, S-751, Swed.

SOURCE: Biochemical and Biophysical Research Communications ( 1998), 248(3), 454-457  
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Osteoprotegerin (OPG) is a recently cloned soluble member of the tumor necrosis factor receptor family. OPG has been shown to inhibit osteoclast recruitment by binding to OPG-ligand, an osteoclast differentiating factor on osteoblastic stromal cells, thereby blocking osteoclastogenesis. Here, the authors examined the effect of tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and tumor necrosis factor- $\beta$  (TNF- $\beta$ ) on OPG mRNA levels in the human osteosarcoma cell line MG-63. The authors demonstrate that both TNF- $\alpha$  and TNF- $\beta$  dose- and time-dependently upregulate the mRNA levels of OPG. The effect is significant at and above 5 pM of TNF- $\alpha$  and 1 pM of TNF- $\beta$ . The stimulatory effect on OPG mRNA levels in MG-63 cells was detected after 2 h of incubation with TNF- $\alpha$  or TNF- $\beta$ . Thus, the expression of OPG in osteoblasts, with subsequent effects on osteoclastogenesis, is regulated by TNFs. (c) 1998 Academic Press.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 30 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 207621-35-0, Osteoclast differentiation factor  
RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence); PROC (Process)  
(mol. cloning of osteoclast differentiation factor, ODF, a ligand for OCIF/OPG)

RN 207621-35-0 CAPLUS

CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 205944-50-9, Osteoclastogenesis-inhibitory factor  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(mol. cloning of osteoclast differentiation factor, ODF, a ligand for OCIF/OPG)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:490782 CAPLUS

DOCUMENT NUMBER: 129:117912

ORIGINAL REFERENCE NO.: 129:24041a,24044a

TITLE: Molecular cloning of osteoclast differentiation factor, ODF (a ligand for OCIF/OPG)

AUTHOR(S): Higashio, Kanji; Shima, Nobuyuki; Yasuda, Hisataka; Suda, Tatsuo

CORPORATE SOURCE: Res. Inst. Life Sci., Snow Brand Milk Prod. Co., Ltd., Tochigi, 329-0512, Japan

SOURCE: Jikken Igaku (1998), 16(11), 1372-1379  
CODEN: JIIGEF; ISSN: 0288-5514

PUBLISHER: Yodosha

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review with 24 refs., on cloning and the structure of osteoclast differentiation factor (ODF) as ligand for osteoclastogenesis inhibitory factor (OCIF)/osteoprotegerin (OPG), binding specificity between ODF and



OCIF, in vitro biol. activity of ODF, ODF target cells, expression of ODF gene and its control, and ODF action in bone tissues. Mol. mechanism of osteoclast differentiation is also discussed.

L11 ANSWER 31 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 205944-50-9, Osteoclastogenesis-inhibitory factor  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)  
(cytokine TR1 (osteoclastogenesis inhibitory factor) sequence, gene mapping, tissue-specific expression, induction of fibroblast proliferation and inhibition of osteoclastogenesis and bone resorption)  
RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:434798 CAPLUS  
DOCUMENT NUMBER: 129:184595  
ORIGINAL REFERENCE NO.: 129:37365a,37368a  
TITLE: TR1, a new member of the tumor necrosis factor receptor superfamily, induces fibroblast proliferation and inhibits osteoclastogenesis and bone resorption  
AUTHOR(S): Kwon, Byoung S.; Wang, S. A.; Udagawa, Nobuyuki; Haridas, Valsala; Lee, Zang H.; Kim, Kack K.; Oh, Kwi-Ok; Greene, John; Li, Yuling; Su, Jeffrey; Gentz, Reiner; Aggarwal, Bharat B.; Ni, Jian  
CORPORATE SOURCE: Department of Microbiology and Immunology, Indiana University School of Medicine and the Walther Cancer Institute, Indianapolis, IN, 46202-5120, USA  
SOURCE: FASEB Journal (1998), 12(10), 845-854  
CODEN: FAJOEC; ISSN: 0892-6638  
PUBLISHER: Federation of American Societies for Experimental Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A newly identified member of the tumor necrosis factor receptor (TNFR) superfamily shows activities associated with osteoclastogenesis inhibition and fibroblast proliferation. This new member, called TR1, was identified from a search of an expressed sequence tag database, and encodes 401 amino acids with a 21-residue signal sequence. Unlike other members of TNFR, TR1 does not contain a transmembrane domain and is secreted as a 62 kDa glycoprotein. TR1 gene maps to chromosome 8q23-24.1 and its mRNA is abundantly expressed on primary osteoblasts, osteogenic sarcoma cell lines, and primary fibroblasts. The receptors for TR1 were detected on a monocytic cell line (THP-1) and in human fibroblasts. Scatchard analyses indicated two classes of high and medium-high affinity receptors with a  $K_D$  of approx. 45 and 320 pM, resp. Recombinant TR1 induced proliferation of human foreskin fibroblasts and potentiated TNF-induced proliferation in these cells. In a coculture system of osteoblasts and bone marrow cells, recombinant TR1 completely inhibited the differentiation of osteoclast-like multinucleated cell formation in the presence of several bone-resorbing factors. TR1 also strongly inhibited bone -resorbing function on dentin slices by mature osteoclasts and decreased  $^{45}\text{Ca}$  release in fetal long-bone organ cultures. Anti-TR1 monoclonal antibody promoted the formation of osteoclasts in mouse marrow culture assays. These results indicate that TR1 has broad biol. activities in fibroblast growth and in osteoclast differentiation and its functions.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 32 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 205944-50-9, Osteoclastogenesis inhibitory factor  
RL: ADV (Adverse effect, including toxicity); BOC (Biological occurrence);  
BSU (Biological study, unclassified); BIOL (Biological study); OCCU  
(Occurrence)  
(severe osteoporosis in mice lacking osteoclastogenesis inhibitory  
factor/osteoprotegerin)  
RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:429241 CAPLUS  
DOCUMENT NUMBER: 129:160204  
ORIGINAL REFERENCE NO.: 129:32593a,32596a  
TITLE: Severe osteoporosis in mice lacking osteoclastogenesis  
inhibitory factor/osteoprotegerin  
AUTHOR(S): Mizuno, Atsuko; Amizuka, Norio; Irie, Kazuharu;  
Murakami, Akihiko; Fujise, Nobuaki; Kanno, Takeshi;  
Sato, Yasushi; Nakagawa, Nobuaki; Yasuda, Hisataka;  
Mochizuki, Shin-ichi; Gomibuchi, Takashi; Yano,  
Kazuki; Shima, Nobuyuki; Washida, Naohiro; Tsuda,  
Eisuke; Morinaga, Tomonori; Higashio, Kanji; Ozawa,  
Hidehiro  
CORPORATE SOURCE: Res. inst. Life Sci., Snow Brand Milk Products, Co.,  
Ltd., Tochigi, 329-0512, Japan  
SOURCE: Biochemical and Biophysical Research Communications ( 1998), 247(3), 610-615  
CODEN: BBRCA9; ISSN: 0006-291X  
PUBLISHER: Academic Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Osteoclasts are multinucleated cells that resorb bone.  
Osteoclastogenesis inhibitory factor (OCIF), also called osteoprotegerin (OPG), acts as a naturally occurring decoy receptor for osteoclast differentiation factor, which mediates an essential signal to osteoclast progenitors for their differentiation into osteoclasts. Here the authors show that the OCIF/OPG knockout mice exhibited severe osteoporosis due to enhanced osteoclastogenesis when they grew to be adults. These mice were viable and fertile. They exhibited marked bone loss accompanied by destruction of growth plate and lack of trabecular bone in their femurs. The strength of their bones dramatically decreased. These results demonstrate that OCIF/OPG is a key factor acting as a neg. regulator against osteoclastogenesis. The OCIF/OPG knockout mice provide the first animal model for osteoporosis without other obvious abnormalities. (c) 1998 Academic Press.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 33 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 205944-50-9, Osteoclastogenesis inhibitory factor  
RL: BPR (Biological process); BSU (Biological study, unclassified); MFM  
(Metabolic formation); BIOL (Biological study); FORM (Formation,  
nonpreparative); PROC (Process)  
(regulation of osteoprotegerin mRNA levels by prostaglandin E2 in human  
bone marrow stroma cells in relation to bone  
resorption)  
RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:420772 CAPLUS  
DOCUMENT NUMBER: 129:131586

ORIGINAL REFERENCE NO.: 129:26785a,26788a

TITLE: Regulation of osteoprotegerin mRNA levels by prostaglandin E2 in human bone marrow stroma cells

AUTHOR(S): Brandstrom, Helena; Jonsson, Kenneth B.; Ohlsson, Claes; Vidal, Olle; Ljunghall, Sverker; Ljunggren, Osten

CORPORATE SOURCE: Department of Internal Medicine, University of Uppsala, Uppsala, S-751 85, Swed.

SOURCE: Biochemical and Biophysical Research Communications ( 1998), 247(2), 338-341  
CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The recently cloned osteoclastogenesis inhibitory factor, or osteoprotegerin (OPG), has been shown to be a potent inhibitor of osteoclast formation. The inhibition is believed to be mediated through specific binding of OPG to a cell surface ligand on osteoblastic stromal cells. In this report we have studied the effect of the bone resorbing agent prostaglandin E2 (PGE2) on OPG mRNA levels in primary cultures of human bone marrow stroma cells (hBMSC). PGE2 dose- and time-dependently down-regulated the mRNA levels of OPG, as measured by RNase protection assay. After 4 h of stimulation with 1  $\mu$ M PGE2, OPG mRNA levels were significantly decreased. The inhibitory effect was seen at and above 1 nM of PGE2. To elucidate whether the OPG mRNA levels are regulated via the protein kinase A and/or the protein kinase C pathways we stimulated cells with either forskolin (FSK) or phorbolic ester (PDbu) resp. FSK (10  $\mu$ M) decreased OPG mRNA levels to 50 % of control, whereas PE (10 nM) upregulated the mRNA levels to 250 % of control. These data show that PGE2 down-regulates the expression of OPG mRNA in hBMSC, probably via an increase in cAMP. This mechanism might be involved in PGE2-induced bone resorption. (c) 1998 Academic Press.

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 34 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoclastogenesis-inhibitory factor  
RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PROC (Process); USES (Uses)  
(regulation and actions of osteoclastogenesis inhibitory factor (OCIF))

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:355267 CAPLUS

DOCUMENT NUMBER: 129:107665

ORIGINAL REFERENCE NO.: 129:22105a,22108a

TITLE: Osteoclastogenesis inhibitory factor (OCIF)

AUTHOR(S): Yasuda, Hisataka

CORPORATE SOURCE: Res. Inst. Life Sci., Snow Brand Milk Prod. Co., Ltd., Tochigi, 329-0512, Japan

SOURCE: Seikagaku (1998), 70(5), 385-390  
CODEN: SEIKAQ; ISSN: 0037-1017

PUBLISHER: Nippon Seikagakkai

DOCUMENT TYPE: Journal; General Review

LANGUAGE: Japanese

AB A review with 7 refs., on purification, structure, regulation of gene expression, mechanism of action, and pharmacol. of osteoclastogenesis-inhibitory factor (OCIF), a member of the TNF receptor family. Utility of OCIF as a therapeutic drug for bone metabolic diseases such as

osteoporosis, is also discussed.

L11 ANSWER 35 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 207621-35-0, Osteoclast differentiation factor

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(osteoclast differentiation factor mediates an essential signal for bone resorption)

RN 207621-35-0 CAPLUS

CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

IT 205944-50-9, Osteoclastogenesis-inhibitory factor

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(osteoclast differentiation factor mediates an essential signal for bone resorption)

RN 205944-50-9 CAPLUS

CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:351157 CAPLUS

DOCUMENT NUMBER: 129:77012

ORIGINAL REFERENCE NO.: 129:15801a,15804a

TITLE: Osteoclast differentiation factor mediates an essential signal for bone resorption induced by  $1\alpha,25$ -dihydroxyvitamin D<sub>3</sub>, prostaglandin E<sub>2</sub>, or parathyroid hormone in the microenvironment of bone

AUTHOR(S): Tsukii, Katsuyoshi; Shima, Nobuyuki; Mochizuki, Shin-Ichi; Yamaguchi, Kyoji; Kinoshita, Masahiko; Yano, Kazuki; Shibata, Osamu; Udagawa, Nobuyuki; Yasuda, Hiroshi; Suda, Tatsuo; Higashio, Kanji

CORPORATE SOURCE: Research Institute of Life Science, Snow Brand Milk Products Co., Ltd., Tochigi, 329-0512, Japan

SOURCE: Biochemical and Biophysical Research Communications (1998), 246(2), 337-341

CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Osteoclast differentiation factor (ODF), a ligand for osteoprotegerin (OPG)/osteoclastogenesis-inhibitory factor (OCIF), induces osteoclast-like cell formation in vitro. To elucidate the role of ODF in the micro-environment of bone, the authors examined effects of ODF, OPG/OCIF, and anti-ODF polyclonal antibody on bone resorption using a fetal mouse long bone culture system. A genetically engineered soluble-form ODF (sODF) elicited bone resorption in a concentration-dependent manner and OPG/OCIF blocked the bone resorption. Anti-ODF polyclonal antibody, which neutralizes ODF activity, negated bone resorption induced by  $1\alpha,25$ -dihydroxyvitamin D<sub>3</sub>, parathyroid hormone, or prostaglandin E<sub>2</sub>. OPG/OCIF also abolished bone-resorbing activity elicited by these bone-resorbing agents. Interleukin  $1\alpha$ -stimulated bone resorption was also significantly suppressed by anti-ODF polyclonal antibody and OPG/OCIF. Thus, the authors conclude that ODF plays a critical role in bone resorption in the microenvironment of bone.

REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 36 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 205944-50-9, Osteoclastogenesis inhibitory factor  
RL: PRP (Properties)  
(identity of osteoclastogenesis inhibitory factor (OCIF) and  
osteoprotegerin (OPG))  
RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:299496 CAPLUS  
Correction of: 1998:133087  
DOCUMENT NUMBER: 128:290635  
Correction of: 128:266572  
ORIGINAL REFERENCE NO.: 128:57450h, 57451a  
TITLE: Identity of osteoclastogenesis inhibitory factor  
(OCIF) and osteoprotegerin (OPG): a mechanism by which  
OPG/OCIF inhibits osteoclastogenesis in vitro  
AUTHOR(S): Yasuda, Hisataka; Shima, Nobuyuki; Nakagawa, Nobuaki;  
Mochizuki, Shin-Ichi; Yano, Kazuki; Fujise, Nobuaki;  
Sato, Yasushi; Goto, Masaaki; Yamaguchi, Kyoji;  
Kuriyama, Masayoshi  
CORPORATE SOURCE: Research Institute of Life Science, Snow Brand Milk  
Products Co., Ltd., Tochigi, 329-0512, Japan  
SOURCE: Endocrinology (1998), 139(3), 1329-1337  
CODEN: ENDOAO; ISSN: 0013-7227  
PUBLISHER: Endocrine Society  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB The morphogenesis and remodeling of bone depends on the  
integrated activity of osteoblasts that form bone and  
osteoclasts that resorb bone. The authors previously reported  
the isolation of a new cytokine termed osteoclastogenesis inhibitory  
factor, OCIF, which specifically inhibits osteoclast development. Here  
the authors report the cloning of a cDNA of human OCIF. OCIF is identical  
to osteoprotegerin (OPG), a soluble member of the tumor-necrosis factor  
receptor family that inhibits osteoclastogenesis. Recombinant human  
OPG/OCIF specifically acts on bone tissues and increases  
bone mineral d. and bone volume associated with a decrease of  
active osteoclast number in normal rats. Osteoblasts or bone  
marrow-derived stromal cells support osteoclastogenesis through  
cell-to-cell interactions. A single class of high affinity binding sites  
for OPG/OCIF appears on a mouse stromal cell line, ST2, in response to  
1,25-dihydroxyvitamin D3. An anti-OPG/OCIF antibody that blocks the  
binding abolishes the biol. activity of OPG/OCIF. When the sites are  
blocked with OPG/OCIF, ST2 cells fail to support osteoclastogenesis.  
These results suggest that the sites are involved in cell-to-cell  
signaling between stromal cells and osteoclast progenitors and that  
OPG/OCIF inhibits osteoclastogenesis by interrupting the signaling through  
the sites.

REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 37 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 207621-35-0, Osteoclast differentiation factor  
RL: BAC (Biological activity or effector, except adverse); BOC (Biological  
occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL  
(Biological study); OCCU (Occurrence)  
(osteoprotegerin ligand as cytokine regulating osteoclast  
differentiation and activation)  
RN 207621-35-0 CAPLUS  
CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1998:288246 CAPLUS  
DOCUMENT NUMBER: 129:258117  
ORIGINAL REFERENCE NO.: 129:52534h,52535a  
TITLE: Osteoprotegerin ligand is a cytokine that regulates osteoclast differentiation and activation  
AUTHOR(S): Lacey, D. L.; Timms, E.; Tan, H. L.; Kelley, M. J.; Dunstan, C. R.; Burgess, T.; Elliott, R.; Colombero, A.; Elliott, G.; Scully, S.; Hsu, H.; Sullivan, J.; Hawkins, N.; Davy, E.; Capparelli, C.; Eli, A.; Qian, Y. X.; Kaufman, S.; Sarosi, I.; Shalhoub, V.; Senaldi, G.; Guo, J.; Delaney, J.; Boyle, W. J.  
CORPORATE SOURCE: Dep. Pathol., Amgen, Inc., Thousand Oaks, CA, 91320-1789, USA  
SOURCE: Cell (Cambridge, Massachusetts) (1998), 93(2), 165-176  
CODEN: CELLB5; ISSN: 0092-8674  
PUBLISHER: Cell Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English  
AB The ligand for Osteoprotegerin has been identified, and it is a TNF-related cytokine that replaces the requirement for stromal cells, vitamin D3, and glucocorticoids in the coculture model of in vitro osteoclastogenesis. OPG ligand (OPGL) binds to a unique hematopoietic progenitor cell that is committed to the osteoclast lineage and stimulates the rapid induction of genes that typify osteoclast development. OPGL directly activates isolated mature osteoclasts in vitro, and short-term administration into normal adult mice results in osteoclast activation associated with systemic hypercalcemia. These data suggest that OPGL is an osteoclast differentiation and activation factor. The effects of OPGL are blocked in vitro and in vivo by OPG, suggesting that OPGL and OPG are key extracellular regulators of osteoclast development.  
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 38 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 205944-50-9, Osteoclastogenesis-inhibitory factor  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(osteoclast differentiation factor is a ligand for osteoprotegerin/osteoclastogenesis-inhibitory factor and is identical to TRANCE/RANKL)  
RN 205944-50-9 CAPLUS  
CN Osteoprotegerin (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
IT 207621-35-0, Osteoclast differentiation factor  
RL: PRP (Properties)  
(osteoclast differentiation factor is a ligand for osteoprotegerin/osteoclastogenesis-inhibitory factor and is identical to TRANCE/RANKL)  
RN 207621-35-0 CAPLUS  
CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*  
ACCESSION NUMBER: 1998:236028 CAPLUS  
DOCUMENT NUMBER: 129:15194  
ORIGINAL REFERENCE NO.: 129:3259a,3262a  
TITLE: Osteoclast differentiation factor is a ligand for osteoprotegerin/osteoclastogenesis-inhibitory factor and is identical to TRANCE/RANKL  
AUTHOR(S): Yasuda, Hisataka; Shima, Nobuyuki; Nakagawa, Nobuaki; Yamaguchi, Kyoji; Kinosaki, Masahiko; Mochizuki,

Shin-Ichi; Tomoyasu, Akihiro; Yano, Kazuki; Goto, Masaaki; Murakami, Akihiko; Tsuda, Eisuke; Morinaga, Tomonori; Higashio, Kanji; Udagawa, Nobuyuki; Takahashi, Naoyuki; Suda, Tatsuo

CORPORATE SOURCE: Research Institute of Life Science, Snow Brand Milk Products Co., Ltd., Tochigi, 329-0512, Japan

SOURCE: Proceedings of the National Academy of Sciences of the United States of America (1998), 95(7), 3597-3602

CODEN: PNASA6; ISSN: 0027-8424

PUBLISHER: National Academy of Sciences

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Osteoclasts, the multinucleated cells that resorb bone, develop from hematopoietic cells of monocyte/macrophage lineage. Osteoclast-like cells (OCLs) are formed by coculturing spleen cells with osteoblast glucosamine 2-N-sulfates or bone marrow stromal cells in the presence of bone-resorbing factors. The cell-to-cell interaction between osteoblasts/stromal cells and osteoclast progenitors is essential for OCL formation. Recently, the authors purified and molecularly cloned osteoclastogenesis-inhibitory factor (OCIF), which was identical to osteoprotegerin (OPG). OPG/OCIF is a secreted member of the tumor necrosis factor receptor family and inhibits osteoclastogenesis by interrupting the cell-to-cell interaction. Here the authors report the expression cloning of a ligand for OPG/OCIF from a cDNA library of mouse stromal cells. The protein was found to be a member of the membrane-associated tumor necrosis factor ligand family and induced OCL formation from osteoclast progenitors. A genetically engineered soluble form containing the extracellular domain of the protein induced OCL formation from spleen cells in the absence of osteoblasts/stromal cells. OPG/OCIF abolished the OCL formation induced by the protein. Expression of its gene in osteoblasts/stromal cells was up-regulated by bone-resorbing factors. The authors conclude that the membrane-bound protein is osteoclast differentiation factor (ODF), a long-sought ligand mediating an essential signal to osteoclast progenitors for their differentiation into osteoclasts. ODF was found to be identical to TRANCE/RANKL, which enhances T-cell growth and dendritic-cell function. ODF seems to be an important regulator in not only osteoclastogenesis but also immune system.

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 39 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 207621-35-0, Osteoclast differentiation factor

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)

(cDNA sequences of mouse and human TRANCE ligand of tumor necrosis factor receptor family activating c-Jun N-terminal kinase in T cells)

RN 207621-35-0 CAPLUS

CN Osteoclast differentiation factor (CA INDEX NAME)

\*\*\* STRUCTURE DIAGRAM IS NOT AVAILABLE \*\*\*

ACCESSION NUMBER: 1997:663234 CAPLUS

DOCUMENT NUMBER: 127:345126

ORIGINAL REFERENCE NO.: 127:67727a,67730a

TITLE: TRANCE is a novel ligand of the tumor necrosis factor receptor family that activates c-Jun N-terminal kinase in T cells

AUTHOR(S): Wong, Brian R.; Rho, Jaerang; Arron, Joseph; Robinson, Elizabeth; Orlinick, Jason; Chao, Moses; Kalachikov, Sergey; Cayani, Eftihia; Bartlett, Frederick S., III; Frankel, Wayne N.; Lee, Soo Young; Choi, Yongwon

CORPORATE SOURCE: Rockefeller University, New York, NY, 10021, USA  
SOURCE: Journal of Biological Chemistry (1997),  
272(40), 25190-25194  
CODEN: JBCHA3; ISSN: 0021-9258  
PUBLISHER: American Society for Biochemistry and Molecular  
Biology  
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB A novel member of the tumor necrosis factor (TNF) cytokine family, designated TRANCE, was cloned during a search for apoptosis-regulatory genes using a somatic cell genetic approach in T cell hybridomas. The TRANCE gene encodes a type II membrane protein of 316 amino acids with a predicted mol. mass of 35 kDa. Its extracellular domain is most closely related to TRAIL, FasL, and TNF. TRANCE is an immediate early gene up-regulated by TCR stimulation and is controlled by calcineurin-regulated transcription factors. TRANCE is most highly expressed in thymus and lymph nodes but not in nonlymphoid tissues and is abundantly expressed in T cells but not in B cells. Cross-hybridization of the mouse cDNA to a human thymus library yielded the human homolog, which encodes a protein 83% identical to the mouse ectodomain. Human TRANCE was mapped to chromosome 13q14 while mouse TRANCE was located to the portion of mouse chromosome 14 syntenic with human chromosome 13q14. A recombinant soluble form of TRANCE composed of the entire ectodomain induced c-Jun N-terminal kinase (JNK) activation in T cells but not in splenic B cells or in bone marrow-derived dendritic cells. These results suggest a role for this TNF-related ligand in the regulation of the T cell-dependent immune response.

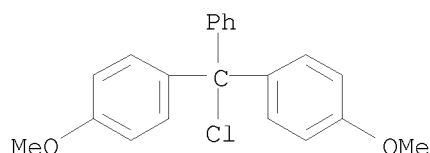
L11 ANSWER 40 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 40615-36-9

RL: RCT (Reactant); RACT (Reactant or reagent)  
(reaction of, with deoxyfluorouridine)

RN 40615-36-9 CAPLUS

CN Benzene, 1,1'-(chlorophenylmethylene)bis[4-methoxy- (CA INDEX NAME)



ACCESSION NUMBER: 1992:648179 CAPLUS

DOCUMENT NUMBER: 117:248179

ORIGINAL REFERENCE NO.: 117:42871a, 42874a

TITLE: Nucleoside-polypeptide conjugates with 3' ester linkage for treatment of tumors and viral diseases

INVENTOR(S): Pietersz, Geoffrey

PATENT ASSIGNEE(S): Austin Research Institute, Australia

SOURCE: PCT Int. Appl., 28 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9214758	A1	19920903	WO 1992-AU47	19920213 <--
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE				



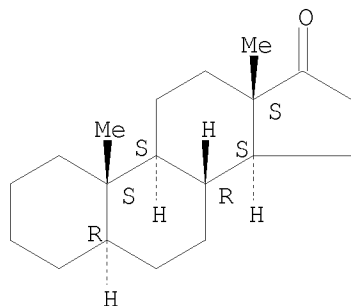
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9202641	A1	19920220	WO 1991-US5690	19910809 <--
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IL 99069	A	19980816	IL 1991-99069	19910802 <--
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AU 9184003	A	19920302	AU 1991-84003	19910809 <--
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JP 06500322	T	19940113	JP 1991-514157	19910809 <--
AT 174063	T	19981215	AT 1991-915657	19910809 <--
AU 9656180	A	19961010	AU 1996-56180	19960625 <--

AU 693690 B2 19980702  
PRIORITY APPLN. INFO.: US 1990-565299 A 19900809  
WO 1991-US5690 A 19910809  
OTHER SOURCE(S): MARPAT 117:66081

AB The title oligonucleotide conjugates are provided, as are reagents (including non-nucleotide linkers) for their preparation. Psoralen-conjugated oligomers complementary to the bcr/abl gene or mRNA are useful in decreasing expression of abl-associated tyrosine kinase and P210 protein. Preparation of the modified oligonucleotides, and of an activated psoralen derivative and of Me phosphonate non-nucleotide linkers of various lengths is included. Crosslinking of a 440-base bcr/abl RNA transcript using a psoralen methylphosphonate oligomer is described.

L11 ANSWER 42 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
IT 963-74-6  
RL: BIOL (Biological study)  
(erythropoiesis stimulation by, in bone marrow)  
RN 963-74-6 CAPLUS  
CN Androstan-17-one, (5 $\alpha$ )- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 1979:468949 CAPLUS  
DOCUMENT NUMBER: 91:68949  
ORIGINAL REFERENCE NO.: 91:11048h,11049a  
TITLE: The influence of steroid hormone metabolites on the in vitro development of erythroid colonies derived from human bone marrow

AUTHOR(S): Urabe, Akio; Sassa, Shigeru; Kappas, Attallah  
CORPORATE SOURCE: Sloan-Kettering Inst. Cancer Res., New York, NY, 10021, USA

SOURCE: Journal of Experimental Medicine (1979), 149(6), 1314-25  
CODEN: JEMEAV; ISSN: 0022-1007

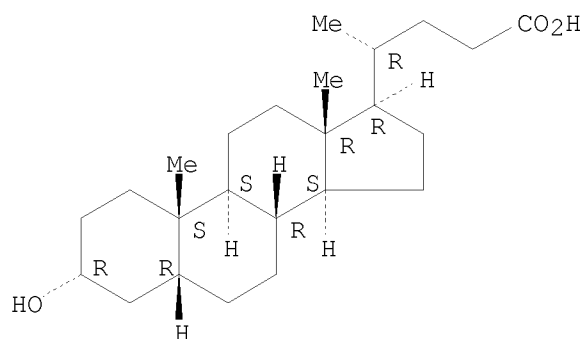
DOCUMENT TYPE: Journal  
LANGUAGE: English

AB Certain C19 and C21 steroid metabolites, when incubated with normal human bone marrow cells in culture, increased the number of erythroid colonies in the presence of erythropoietin [11096-26-7]. Among a number of pairs of C5 epimeric steroids tested, most 5 $\beta$  (A:B cis) steroids stimulated the growth of both early erythroid progenitor cells (BFU-E) and late erythroid progenitor cells (CFU-E), whereas only a few 5 $\alpha$ -(A:B trans) steroids stimulated the growth of CFU-E. No 5 $\alpha$ -comps. of 6 pairs of steroids studied stimulated BFU-E formation. This structure-activity relation conforms with that previously observed in studies of steroid induction of  $\delta$ -aminolevulinic acid synthetase in avian embryo liver cells and Hb synthesis in the cultured avian blastoderm. When human bone marrow cells were preincubated with the steroids for 2 d, followed by incubation with erythropoietin, only the

5 $\beta$ -compds. stimulated the growth of BFU-E. Similarly, when addition of steroids was delayed in relation to erythropoietin in the culture, only the 5 $\beta$ -derivative of a pair of C5 epimeric compds. displayed an enhancing effect on the growth of BFU-E. This effect required that the steroid addition be made no later than 48 h after initiation of the culture. Thus, certain natural steroid metabolites stimulate erythropoiesis in normal human bone marrow cells in culture. 5 $\beta$ -Compds. are more stimulatory than their 5 $\alpha$ -epimers, and these 5 $\beta$ -steroids act preferentially on very primitive erythroid progenitor cells, probably on BFU-E.

L11 ANSWER 43 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
 IT 434-13-9  
 RL: BIOL (Biological study)  
 (hemoglobin formation by bone marrow in response to)  
 RN 434-13-9 CAPLUS  
 CN Cholan-24-oic acid, 3-hydroxy-, (3 $\alpha$ ,5 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.



ACCESSION NUMBER: 1974:433634 CAPLUS  
 DOCUMENT NUMBER: 81:33634  
 ORIGINAL REFERENCE NO.: 81:5365a,5368a  
 TITLE: Effect of certain 5 $\beta$ -H steroid metabolites on hemoglobin synthesis in cultured human marrow cells  
 AUTHOR(S): Levere, Richard D.; Mizoguchi, Hideaki  
 CORPORATE SOURCE: Downstate Med. Cent., State Univ. New York, Brooklyn, NY, USA  
 SOURCE: Androgens Anemia Bone Marrow Failure, Proc. Symp. (1971), Meeting Date 1971, 15-20. Editor(s): Necheles, Thomas F. Syntex Lab., Inc.: Palo Alto, Calif.  
 CODEN: 28EHAR  
 DOCUMENT TYPE: Conference  
 LANGUAGE: English  
 AB 5 $\beta$ -H steroids (11-ketopregnanolone (I) [565-99-1], etiocholanolone [53-42-9], and pregnanediol [80-92-2]), but not their 5 $\alpha$ -H epimers, stimulated heme and globin synthesis by bone marrow cells. There were indications that the effects of the steroids required the de novo synthesis of both RNA and proteins. Structure-activity relations are discussed.

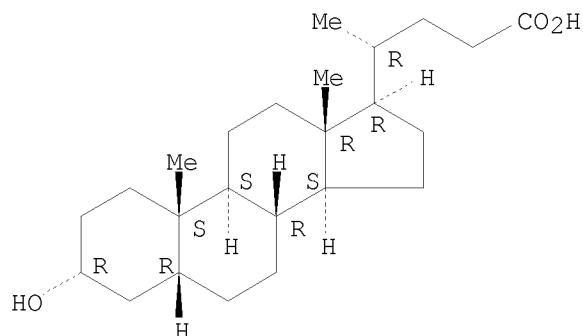
L11 ANSWER 44 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
 ACCESSION NUMBER: 1972:54548 CAPLUS  
 DOCUMENT NUMBER: 76:54548  
 ORIGINAL REFERENCE NO.: 76:8753a,8756a  
 TITLE: Enhancemet of heme and globin synthesis in cultured human marrow by certain 5 $\beta$ -H steroid metabolites

AUTHOR(S): Mizoguchi, Hideaki; Levere, Richard D.  
 CORPORATE SOURCE: Downstate Med. Cent., State Univ. New York, Brooklyn, NY, USA  
 SOURCE: Journal of Experimental Medicine (1971), 134(6), 1501-12  
 CODEN: JEMEAV; ISSN: 0022-1007  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB Of the 9 steroids tested, 3 .tim. 10-3 M 5 $\beta$ -pregnan-3 $\alpha$ -ol-11,20-dione [565-99-1], etiocholanolone [53-42-9], and 5 $\beta$ -pregnanediol [80-92-2] stimulated heme [14875-96-8] and globin synthesis in cultured human bone marrow cells; 5 $\alpha$ -pregnane-3 $\alpha$ -ol-11,20-dione [23930-19-0], 5 $\alpha$ -pregnanediol [566-58-5], etiocholanolone glucuronide [3602-09-3], progesterone [57-83-0], testosterone [58-22-0], and lithocholic acid [434-13-9] had no such effect. Low concns. of either actinomycin D [50-76-0] or puromycin [53-79-2], abolished the stimulating effects of the active steroids, suggesting that the action of 5 $\beta$ -H steroids on Hb formation required both new RNA and new protein synthesis. This steroid action was independent of erythropoietin, and since these compds. are effective at such low concns. they may have a physiol. role in the regulation of human erythropoiesis.

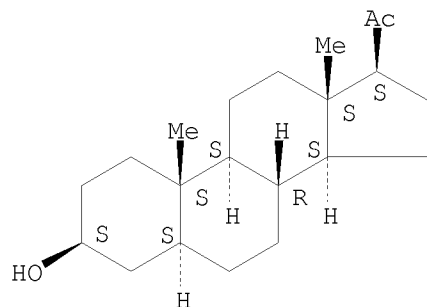
L11 ANSWER 45 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN  
 IT 434-13-9 516-55-2  
 RL: BIOL (Biological study)  
 (erythropoiesis in response to, in mice)  
 RN 434-13-9 CAPLUS  
 CN Cholan-24-oic acid, 3-hydroxy-, (3 $\alpha$ ,5 $\beta$ )- (CA INDEX NAME)

Absolute stereochemistry.



RN 516-55-2 CAPLUS  
 CN Pregnan-20-one, 3-hydroxy-, (3 $\beta$ ,5 $\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



ACCESSION NUMBER: 1970:412558 CAPLUS  
 DOCUMENT NUMBER: 73:12558  
 ORIGINAL REFERENCE NO.: 73:2093a,2096a  
 TITLE: Erythropoietic activity of steroid metabolites in mice  
 AUTHOR(S): Gorshein, D.; Gardner, Frank H.  
 CORPORATE SOURCE: Med. Center, Presbyterian-Univ. of Pennsylvania,  
 Philadelphia, PA, USA  
 SOURCE: Proceedings of the National Academy of Sciences of the  
 United States of America (1970), 65(3),  
 564-8  
 CODEN: PNASA6; ISSN: 0027-8424  
 DOCUMENT TYPE: Journal  
 LANGUAGE: English

AB The percent  $^{59}\text{Fe}$  incorporation into circulating erythrocytes as an indicator for new Hb production was used in the polycythemic exhypoxic mouse system to study the effects of certain steroid hormone metabolites on erythropoiesis. Enhanced  $^{59}\text{Fe}$  incorporation was observed after the administration of several metabolites with a  $5\beta\text{-H}$  configuration, while those with a  $5\alpha\text{-H}$  configuration had no stimulatory effect. The stimulatory effect in avian systems is due to an increased activity of  $\delta$ -aminolevulinic acid synthetase, the limiting enzyme in heme biosynthesis. These in vivo studies thus indicate that in this mouse system, as in previously reported studies with avian and human bone marrow cells, some steroid metabolites stimulate Hb synthesis. The observation that the same structure-junction relation exists in the currently described system as in the avian suggests that these steroids probably induce  $\delta$ -aminolevulinic acid synthetase in the mouse. The erythropoietic action of these nonadrogenic steroid metabolites may prove to be clin. useful.

L11 ANSWER 46 OF 46 CAPLUS COPYRIGHT 2008 ACS on STN

IT 516-55-2

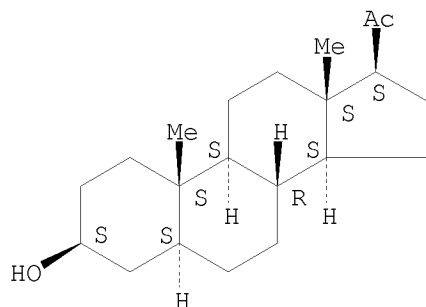
RL: BIOL (Biological study)

(cartilage growth and nitrogen content in culture in response to)

RN 516-55-2 CAPLUS

CN Pregnan-20-one, 3-hydroxy-, ( $3\beta,5\alpha$ )- (CA INDEX NAME)

Absolute stereochemistry. Rotation (+).



ACCESSION NUMBER: 1967:479291 CAPLUS  
 DOCUMENT NUMBER: 67:79291  
 ORIGINAL REFERENCE NO.: 67:14934h,14935a  
 TITLE: Effect of progesterone and progesterone metabolites on  
 the growth of embryonic cartilage in vitro  
 AUTHOR(S): Schaer, Bertha  
 CORPORATE SOURCE: CIBA A.-G., Basel, Switz.  
 SOURCE: Experientia (1967), 23(9), 716-17  
 CODEN: EXPEAM; ISSN: 0014-4754

DOCUMENT TYPE: Journal  
LANGUAGE: German

AB At 1  $\gamma$ /ml. of medium, progesterone, 5 $\beta$ -dihydroprogesterone, 3 $\alpha$ -hydroxy-5 $\beta$ -tetrahydroprogesterone, and 20 $\beta$ -hydroxydihydroprogesterone reduced the total dry weight of embryonic chick femur and tibia cultured in vitro to a greater extent than they did the weight of the N-containing portion of the cartilage. 11 $\beta$ -Hydroxyprogesterone did not decrease dry weight and slightly increased the N content. 5 $\alpha$ -Dihydroprogesterone, 3 $\beta$ -hydroxy-5 $\beta$ -tetrahydroprogesterone, 3 $\alpha$ -hydroxy-5 $\alpha$ -tetrahydroprogesterone, 20 $\alpha$ -hydroxydihydroprogesterone, 17 $\alpha$ -hydroxyprogesterone, and 11 $\beta$ ,17 $\alpha$ -dihydroxyprogesterone slightly inhibited bone growth without increasing the N-containing portion in the cartilage.

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